

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Jeffrey E. Russell Examiner #: 52725 Date: 5-9-2003
 Art Unit: 659 Phone Number 308-3975 Serial Number: 09780943
 Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle) PAPER DISK E-MAIL
CM-11013/CM-9807

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

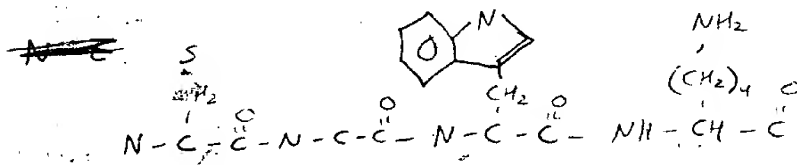
Title of Invention: Somatostatin Agonists

Inventors (please provide full names): D. Sadat-Aalace, B. Morgan

Earliest Priority Filing Date: 2-22-2002

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search the following structure:



Please use the term "somatostatin" to narrow any hits.

Please exclude WO 01/00676 and US 6,262,229 and WO 98/24807 from any answer sets.

Thank you.

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	Type of Search	Vendors and cost where applicable
Searcher: <u>Shiragami</u>	NA Sequence (#) _____	STN _____
Searcher Phone #: <u>308-4149</u>	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: _____	Bibliographic _____	Dr. Link _____
Date Completed: <u>5/9/03</u>	Litigation _____	Lexis/Nexis _____
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Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: _____	Other _____	Other (specify) _____

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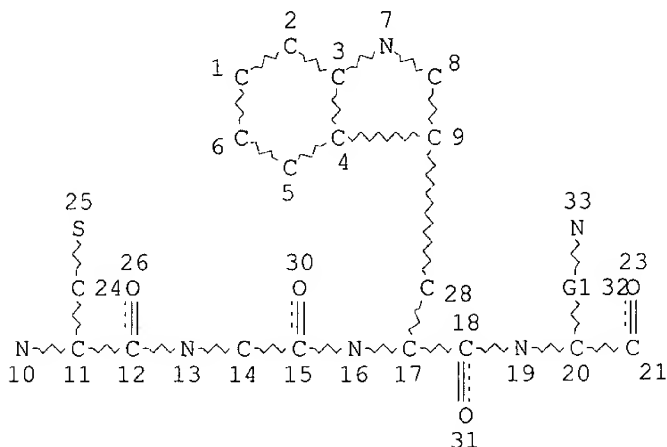
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FILE COVERS 1907 - 9 May 2003 VOL 138 ISS 20
 FILE LAST UPDATED: 8 May 2003 (20030508/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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 L1 STR



REP G1=(4-4) C
 NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

L3 576 SEA FILE=REGISTRY SSS FUL L1
 L4 1206 SEA FILE=REGISTRY ABB=ON PLU=ON SOMATOSTATIN
 L5 240 SEA FILE=HCAPLUS ABB=ON PLU=ON L3
 L6 17330 SEA FILE=HCAPLUS ABB=ON PLU=ON L4 OR ?SOMATOSTAT?
 L8 48 SEA FILE=HCAPLUS ABB=ON PLU=ON L5(L)L6

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L8 ANSWER 1 OF 48 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2003:282298 HCAPLUS
 DOCUMENT NUMBER: 138:297698
 TITLE: Somatostatin or bombesin analog conjugates, and
 therapeutic and diagnostic uses thereof
 INVENTOR(S): Coy, David H.; Fuselier, Joseph A.; Murphy, William
 A.; Sun, Lichun
 PATENT ASSIGNEE(S): The Administrators of the Tulane Educational Fund, USA
 SOURCE: PCT Int. Appl., 86 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003028527	A2	20030410	WO 2002-US30143	20020920
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2001-323851P P 20010921

AB The invention discloses somatostatin and bombesin analog conjugates and
 uses thereof for targeting compds. useful for detection, diagnosis, and
 treatment of diseases. The peptide agents of the invention include XYZQ
 (X = cytotoxic agent, detectable label, etc., or is omitted; Y = peptide
 increasing hydrophilic biodistribution of agent, hydrophilic polymer
 including linker for X, omitted; Z = linking peptide; Q = peptide with
 biol. activity, e.g. somatostatin peptide).

IT 507442-16-2D, conjugates with Methotrexate 507442-17-3D,
 conjugates with Methotrexate 507442-18-4D, conjugates with
 Methotrexate
 RL: DGN (Diagnostic use); PAC (Pharmacological activity); PRP
 (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (somatostatin or bombesin analog conjugates, and therapeutic
 and diagnostic uses thereof)

IT 442685-60-1 508194-86-3 508194-87-4
 508194-88-5 508194-89-6 508194-90-9
 508194-91-0
 RL: PRP (Properties)
 (unclaimed sequence; somatostatin or bombesin analog
 conjugates, and therapeutic and diagnostic uses thereof)

L8 ANSWER 2 OF 48 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:971469 HCAPLUS
 DOCUMENT NUMBER: 138:231967
 TITLE: Demonstration of enhanced potency of a chimeric
 somatostatin-dopamine molecule, BIM-23A387, in

AUTHOR(S): suppressing growth hormone and prolactin secretion from human pituitary somatotroph adenoma cells
Saveanu, A.; Lavaque, E.; Gunz, G.; Barlier, A.; Kim, S.; Taylor, J. E.; Culler, M. D.; Enjalbert, A.; Jaquet, P.

CORPORATE SOURCE: Interactions Cellulaires Neuroendocriniennes, Unite Mixte de Recherche 6544, Centre National de la Recherche Scientifique Institut Federatif Jean Roche, Faculte de Medecine Nord, Marseille, 13916/20, Fr.

SOURCE: Journal of Clinical Endocrinology and Metabolism (2002), 87(12), 5545-5552
CODEN: JCEMAZ; ISSN: 0021-972X

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In acromegaly, the combination of somatostatin (SS) and dopamine (DA) agonists has been shown to enhance suppression of GH secretion. In the present study, a new chimeric mol., BIM-23A387, which selectively binds to the SS subtype 2 receptor (sst2; Ki = 0.10 nM) and to the DA D2 receptor (D2DR; Ki = 22.1 nM) was tested in cultures prep. from 11 human GH-secreting tumors for its ability to suppress GH and prolactin (PRL) secretion. The chimeric compd. was compared with individual sst2 and D2DR agonists of comparable activity at the individual receptors. All tumors expressed both sst2 and D2DR mRNAs (0.8+-.0.2 and 4.7+-.0.7 copy/copy .beta.-glucuronidase mRNA, resp.). In cell cultures from seven octreotide-sensitive tumors, the maximal inhibition of GH release induced by the individual sst2 and D2DR analogs and by BIM-23A387 was similar. However, the mean EC50 for GH suppression by BIM-23A387 (0.2 pM) was 50 times lower than that of the individual sst2 and D2DR analogs, either used individually or combined. Similar data were obtained in four tumors that were only partially responsive to octreotide. The inhibition of GH release by BIM-23A387 was only partially reversed by the D2R2 antagonist, sulpiride, or by the sst2 antagonist, BIM-23454. Only when both antagonists were combined was the GH suppressive effect of BIM-23A387 totally reversed. Finally, BIM-23A387 produced a mean 73+-.6% inhibition of PRL in six mixed GH plus PRL tumors. These data demonstrate an enhanced potency of the chimeric mol., BIM-23A387, in suppressing GH and PRL secretion from acromegalic tumors, which cannot be explained merely on the basis of binding affinity for SS and/or DA receptors.

IT 243470-86-2, BIM-23454 #
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(demonstration of enhanced potency of chimeric **somatostatin** -dopamine mol. BIM-23A387 in suppressing growth hormone and prolactin secretion from human pituitary somatotroph adenoma cells)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:964383 HCAPLUS

DOCUMENT NUMBER: 138:39546

TITLE: Preparation of somatostatin-dopamine chimeric analogs

INVENTOR(S): Culler, Michael D.; Dong, Zheng Xin; Kim, Sun H.; Moreau, Jacques-Pierre

PATENT ASSIGNEE(S): Societe de Conseils de Recherches et d'Applications Scientifiques S.A.S., Fr.

SOURCE: PCT Int. Appl., 170 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

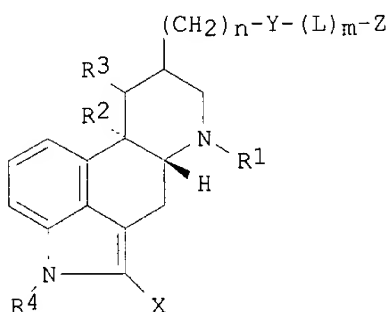
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100888	A1	20021219	WO 2002-US17859	20020607

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-297059P P 20010608
 OTHER SOURCE(S): MARPAT 138:39546
 GI



I

AB Disclosed is a series of somatostatin-dopamine chimeric analogs, e.g., I [X = H, Cl, Br, I, F, -CN, or alkyl; R1 = H, alkyl, allyl, alkenyl or -CN; R2, R3 = H or absent and a double bond is present between the carbon atoms to which they are attached; R4 = H or Me; Y = O, CO, S, S(CH2)0-10CO, SO, SO2, SCO, OCO, NR5CO, or NR6, where R5, R6 = H or alkyl; m = 0 or 1; n = 0-10; L = (CH2)1-10-CO when Y is S, SO, SO2, O, or NR6, L is CO(CR7R8)2-4CO (R7, R8 = H or alkyl) when Y is NR6, O, or S, and L is (Doc)1-10 (Doc = 8-amino-3,6-dioxaoctanoyl) when Y is CO, SCO, O2C, S(CH2)1-10, or NR6CO; Z = is a somatostatin analog or a moiety H, OH, alkoxy, arylalkoxy, or NR9R10, where R9, R10 = H or alkyl] or their pharmaceutically-acceptable salts, which retain both somatostatin and dopamine activity in vivo. An example is 6-n-propyl-8.beta.-ergolylmethylthioacetyl-D-Phe-cyclo(Cys-Tyr-D-Trp-Lys-Abu-Cys)-Thr-NH2 (Abu = 2-aminobutanoic acid), which was prep'd. by the solid-phase method using Fmoc chem.

IT 478815-13-3D, resin-bound 478815-15-5D, resin-bound
 478815-17-7D, resin-bound 478815-19-9D, resin-bound
 478815-21-3D, resin-bound 478815-32-6D, resin-bound
 478815-33-7D, resin-bound 478815-34-8D, resin-bound
 478815-35-9D, resin-bound 478815-36-0D, resin-bound
 478815-37-1D, resin-bound 478815-38-2D, resin-bound
 478815-39-3D, resin-bound
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (prepn. of somatostatin-dopamine chimeric analogs)

IT 478815-31-5DP, resin-bound
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. of somatostatin-dopamine chimeric analogs)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:932090 HCAPLUS
DOCUMENT NUMBER: 138:180916
TITLE: Somatostatin, its receptors, analogues and action mechanisms
AUTHOR(S): Cimen, Burak; Atik, Ugur
CORPORATE SOURCE: Turk.
SOURCE: Turk Biyokimya Dergisi (2002), 27(3), 112-120
CODEN: TBDUAL; ISSN: 0250-4685
PUBLISHER: Turk Biyokimya Dergisi
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Turkish

AB A review. Somatostatin (S) which is named GHRIH was first discovered by Krulich et al in 1968. S is secreted in two different active forms; a 14 amino acid peptide and a 28 amino acid peptide. In mammals, these products are generated by endoproteolytic processing of prosomatostatin at two distinct regions at the C terminal region. Serine proteases have an important role in these process. Six members of these family have been identified in mammals: Furin, PC1-6. Furin has a mediated role in monobasic processing which is named S-28 convertase. Both PC1 and PC2 have a role in dibasic processing of prosomatostatin. PC1 is named S-14 convertase. Five different S receptor (SR) genes have been described SR can be divided into two different groups. The SR-I group (which consists SR2,3,5) can be differentiated from SR-II group (which consists S1,4). Moreover SR2 subgroup has two variants named SR2A and SR2B. The physiol. action of SR is mediated by adeny cyclase throughout specific membrane bound G protein coupled receptors, phospholipase C, calcium and potassium channels, protein tyrosine phosphatase, phospholipase A2. S inhibits release of insulin, glucagon, gastrin, cholecystokinin, secretin, VIP, gastric inhibitory peptide, motilin, enteroglucagon, neurotensin and substance-P in gastrointestinal tract besides inhibition of GH and TSH in endocrine system. The use of natural S is not practical, because of the necessity of iv. use, short effect period and hypersecretion after the infusion. In Rhesus monkeys, octreotide inhibits GH (45 folds), glucagon (11 folds) and insulin (1,3 folds) more than S and octreotide has not hypersecretion side effect. There are different analogs of S (vapeptide, lantreotide) in clin. practice. The therapeutical use of S analogs is approved in carcinoid syndrome, pancreatic endocrine tumors and acromegaly in USA and European countries.

IT 132609-33-7, Lantreotide

RL: PAC (Pharmacological activity); BIOL (Biological study)
(somatostatin, somatostatin processing,
somatostatin receptors, somatostatin analogs and
action mechanisms)

L8 ANSWER 5 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:832658 HCAPLUS
DOCUMENT NUMBER: 137:334689
TITLE: Tc and Re labeler radioactive glycosylated octreotide derivatives
INVENTOR(S): Wester, Hans-Jurgen; Schottelius, Margret; Schwaiger, Markus
PATENT ASSIGNEE(S): Mallinckrodt Inc., USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085418	A2	20021031	WO 2002-US12565	20020423

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2001-201466 A 20010423

AB Improved sst-receptor binding peptidic ligands for diagnostic and therapeutic applications in nuclear medicine are provided. The improved ligands contain either natural or unnatural amino acids or peptidomimetic structures that are modified at either the N-terminal or the C-terminal end or at both termini, a carbohydrate unit and a chelator or prosthetic group to provide a complexation of a radioisotope binding or holding the radioisotope. The sst- or SSTR- receptor binding peptidic ligands may also contain one or more multifunctional linker units optionally coupling the peptide, and/or the sugar moiety and/or the chelator and/or the prosthetic group. Upon administering the ligand to a mammal through the blood system the ligand provides improved availability, clearance kinetics, sst-receptor targeting and internalization over the non-carbohydrated ligands.

IT 473931-63-4 473931-63-4D, Maltotriose/glucose derivs.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**somatostatin** receptor binding peptidic ligands for
diagnostic and therapeutic applications in nuclear medicine)

L8 ANSWER 6 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:793646 HCAPLUS

DOCUMENT NUMBER: 137:295256

TITLE: Preparation of cyclic peptides as somatostatin agonists

INVENTOR(S): Coy, David H.; Rajeswaran, Walajapet G.

PATENT ASSIGNEE(S): The Administrators of the Tulane Educational Fund, USA

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002081499	A2	20021017	WO 2002-US10882	20020408

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-282526P P 20010409

OTHER SOURCE(S): MARPAT 137:295256

AB The invention is directed to cyclic peptides A1-cyclo[Cys-A2-D-Trp-A3-A4-Cys]-A5-Y1 [A1 is an optionally-substituted D- or L-arom. .alpha.-amino acid or D- or L-cyclo(C3-6)alkylalanine; A2 is an optionally-substituted arom. .alpha.-amino acid or cyclo(C3-6)alkylalanine; A3 is Lys or Orn; A4, A5 = .beta.-hydroxyvaline, Ser, hSer, or Thr; Y1 is OH, NH2 or alkylamino;

the substituent on the arom. vsigma.-amino acid or cyclo(C3-6)alkylalanine is selected from halogen, NO₂, OH, CN, alkyl, alkenyl, alkynyl, alkoxy, Bzl, O-Bzl, or an amino group; the amine nitrogen of each amide peptide bond and the amino group of A1 is optionally substituted with a Me group (there is at least one Me group)] and their pharmaceutically-acceptable salts for use as somatostatin agonists. The solid-phase method was applied to the synthesis of 18 cyclic peptides of the invention, including NMe-D-Phe-cyclo[Cys-Phe-D-Trp-Lys-Thr-Cys]-Thr-NH₂ (1). Peptide 1 showed binding affinities K_d for cloned human sst1-5 receptors of 316 .+-. 11, 1.03 .+-. 0.26, 17.9 .+-. 2.5, >1.000, and 4.89 .+-. 1.4 nM, resp., and agonist activity IC₅₀ = 0.32 .+-. 0.13 nM on culture rat pituitary cells.

IT **204387-96-2DP**, N-Me derivs.

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of cyclic peptides as **somatostatin** agonists)

L8 ANSWER 7 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:540254 HCAPLUS

DOCUMENT NUMBER: 137:99024

TITLE: Use of somatostatin analogs for the delivery of anti-tumor drugs to tumor cells

INVENTOR(S): Chen, Shui-tein; Wu, Ying-ta; Huang, Chun-ming

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 482,451, abandoned.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002094964	A1	20020718	US 2000-734298	20001211
US 6552007	B2	20030422		

PRIORITY APPLN. INFO.: US 2000-482451 B2 20000113

OTHER SOURCE(S): MARPAT 137:99024

AB A conjugate of somatostatin-spacer-drug and a method of making the same are given. The conjugate can be used to enhance an anti-cancer drug's specificity on the targeted tumor cells, thus increasing its therapeutic efficacy while reducing side-effects. Paclitaxel-glutaryl-octreotide was prepd. from paclitaxel, glutaric anhydride and solid-phase peptide synthesis of octreotide. Octreotide-conjugated paclitaxel induced only the death of MCF-7 cells but not CHO cells.

IT **442685-60-1 442685-61-2**

RL: PRP (Properties)

(unclaimed sequence; use of **somatostatin** analogs for the delivery of anti-tumor drugs to tumor cells)

IT **441788-19-8DP**, Acetal, resin-bound **441788-20-1DP**,

Acetal, resin-bound

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(use of **somatostatin** analogs for delivery of anti-tumor drugs to tumor cells)

L8 ANSWER 8 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:302140 HCAPLUS

DOCUMENT NUMBER: 137:43585

TITLE: NODAGATOC, a New Chelator-Coupled Somatostatin Analogue Labeled with [67/68Ga] and [111In] for SPECT, PET, and Targeted Therapeutic Applications of

AUTHOR(S): Somatostatin Receptor (hsst2) Expressing Tumors
Eisenwiener, Klaus-Peter; Prata, M. I. M.; Buschmann,
I.; Zhang, Han-Wen; Santos, A. C.; Wenger, Sandra;
Reubi, Jean Claude; Maecke, Helmut R.

CORPORATE SOURCE: Division of Radiological Chemistry, Institute of
Nuclear Medicine, Department of Radiology, University
Hospital, Basel, CH-4031, Switz.

SOURCE: Bioconjugate Chemistry (2002), 13(3), 530-541
CODEN: BCCHE; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A monoreactive NOTA (1,4,7-triazacyclononane-1,4,7-triacetic acid) derived
prochelator (1-(1-carboxy-3-carbo-tert-butoxypropyl)-4,7-(carbo-tert-
butoxymethyl)-1,4,7-triazacyclononane (NODAGA(tBu)3)) was synthesized in
five steps with an overall yield of 21%. It is useful for the coupling to
the N-terminus of peptides on solid phase and in soln.; it was coupled to
[Tyr3]-octreotide (TOC) on solid phase, and the resulting peptide,
NODAGA-Tyr3-octreotide (NODAGATOC), was labeled with the radiometals ¹¹¹In
and ⁶⁷Ga in high yields and good specific activities. [⁶⁷Ga]- and
[¹¹¹In]-NODAGA-Tyr3-octreotide appear to be useful to visualize primary
tumors and metastases which express somatostatin receptors subtype 2
(sstr2), such as neuroendocrine tumors, because of their high affinity to
this receptor subtype with IC50 = 3.5 +/- 1.6 nM and 1.7 +/- 0.2 nM,
resp. NODAGATOC could be used as a SPECT and PET tracer, when labeled
with ¹¹¹In, ⁶⁷Ga, or ⁶⁸Ga, and even for therapeutic applications.
Surprisingly, [¹¹¹In]-NODAGATOC shows 2 times higher binding affinity to
sstr2, but also a factor of 4 higher affinity to sstr5 compared to
[⁶⁷Ga]-NODAGATOC. [⁶⁷Ga]-NODAGATOC is very stable in serum and rat liver
homogenate. There is no difference in the rate of internalization into
AR4-2J rat pancreatic tumor cells; both radioligands are highly
internalized, at 4 h a 3 times higher uptake compared to
[¹¹¹In]-DOTA-Tyr3-octreotide ([¹¹¹In]-DOTATOC) was found. The
biodistribution of [⁶⁷Ga]-NODAGATOC in AR4-2J tumor bearing nude mice is
very favorable at short times after injection; there is fast excretion
from all nontarget organs except the kidneys and high uptake in sst
receptor rich organs and in the AR4-2J tumor. Again it is superior to
[¹¹¹In]-DOTATOC in this respect. The results indicate an improved biol.
behavior which is likely due to the fact that an addnl. spacer group
separates the chelate from the pharmacophoric part of the somatostatin
analog.

IT 438526-79-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(NODAGATOC (NODAGA-Tyr3-octreotide): chelator-coupled ⁶⁷Ga- and
¹¹¹In-labeled **somatostatin** analog for SPECT, PET, and
targeted radiotherapy of **somatostatin** receptor-expressing
tumors)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:255106 HCAPLUS

DOCUMENT NUMBER: 136:396194

TITLE: Characterization of new selective somatostatin
receptor subtype-2 (sstr2) antagonists, BIM-23627 and
BIM-23454. Effects of BIM-23627 on GH release in
anesthetized male rats after short-term high-dose
dexamethasone treatment

AUTHOR(S): Tulipano, G.; Soldi, D.; Bagnasco, M.; Culler, M. D.;
Taylor, J. E.; Cocchi, D.; Giustina, A.

CORPORATE SOURCE: Department of Biomedical Sciences and Biotechnology,
University of Brescia, Brescia, 25125, Italy

SOURCE: Endocrinology (2002), 143(4), 1218-1224

CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We here report a pharmacol. characterization of two new somatostatin (SS) receptor subtype-2 (sst2) selective antagonists by evaluating their GH-releasing activity when administered, by different routes, in anesthetized adult rats and in freely moving 10-d-old rats. Moreover, we describe the effect of these SS antagonists on the GH response to GHRH after short-term high-dose dexamethasone (DEX) treatment in young male rats. BIM-23454 and BIM-23627, given i.v., were able to counteract the SS-induced inhibition of GH secretion occurring after urethane anesthesia in a dose-dependent manner. In DEX-treated animals, the GH response to GHRH was partially blunted (5-min peak values, 270 ng/mL in saline-treated vs. 160 ng/mL in DEX-treated); however, the simultaneous administration of BIM-23627 (0.2 mg/kg, i.v.) restored higher amplitude GH pulse, leading to a significantly higher overall mean GH response (area under the curve, 4200 ng/mL/30 min vs. 2800 ng/mL/30 min after GHRH alone). The SS antagonists showed a reduced GH-releasing effect when administered s.c. or i.p., likely attributable to decreased bioavailability, as compared with the iv route. SS antagonist administration also increased plasma glucagon, insulin, and glucose levels. Based on prior reports that sst2 tonically suppresses glucagon secretion, the antagonist most likely increased glucagon secretion from the pancreatic .alpha.-cells, with resultant increases in plasma glucose and then insulin.

IT 243470-86-2, BIM-23454

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PAC (Pharmacological activity); BIOL (Biological study);
USES (Uses)

(somatostatin receptor subtype-2 antagonists effects on growth hormone release in anesthetized male rats after short-term high-dose dexamethasone treatment)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:211774 HCAPLUS

DOCUMENT NUMBER: 137:211269

TITLE: Human urotensin II-induced aorta ring contractions are mediated by protein kinase C, tyrosine kinases and Rho-kinase: inhibition by somatostatin receptor antagonists

AUTHOR(S): Rossowski, Wojciech J.; Cheng, Beng-L.; Taylor, John E.; Datta, Rakesh; Coy, David H.

CORPORATE SOURCE: Department of Medicine, Peptide Research Laboratories, Tulane University Medical Science Center, New Orleans, LA, 70112, USA

SOURCE: European Journal of Pharmacology (2002), 438(3), 159-170

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human urotensin II-(1-11) and its N-terminally shortened analogs, human urotensin II-(4-11)-OH and human urotensin II-(4-11)-NH₂ are potent vasoconstrictor peptides in isolated rat thoracic aorta. Human urotensin II-induced tonic aorta ring contractions are inhibited by the Ca²⁺ channel antagonists, verapamil, nitrendipine and diltiazem; D609 (Tricyclodecan-9-yl-xanthogenate, K), selective inhibitor of phosphatidylcholine-specific phospholipase C and partially by phospholipase C inhibitor U-73122 {1-[6-((17.beta.-3 Methoxyestra-1,3,5(10)-trien-17-yl)amino)hexyl]-1H-pyrrole-25-dione} and a selective inhibitor of phosphatidyl-inositol-specific phospholipase C-ET-18-OCH₃

(Edelfosine, 1-O-octadecyl-20-methyl-rac-glycero-3-phosphorylcholine); protein kinase C inhibitors, chelerythrine and NPC-15437 {S-2,6-diamino-N-[[1-(1-oxotridecyl)-2-piperidiny]methyl]-hexanamide dihydrochloride}; tyrosine kinase inhibitors, genistein and tyrphostin B42 and Rho-kinase inhibitor HA-1077 [1-(5-isoquinoliny)sulfonyl]-homopiperazine dihydrochloride]. This indicates that human urotensin II-induced tonic contractions of the rat aorta are mediated by phospholipase C, protein kinase C, tyrosine kinases and Rho-kinase related pathways. In the high K⁺ medium, human urotensin II induces dose-dependent phasic oscillations of aortic rings. These are inhibited by Ca²⁺ channel antagonists, the phospholipase C inhibitor, U-73122 and protein kinase C inhibitors, chelerythrine and NPC-15437, indicating that human urotensin II-induced phasic oscillations of the rat aorta are mediated by phospholipase C and protein kinase C-dependent pathways. Given their close structural similarity, several somatostatin analogs, importantly contg. DCys5 and DTrp7 and expressing different degrees of somatostatin receptor antagonist activity, were tested for possible inhibitory effects on human urotensin II-induced contractions of the rat aorta rings. Pre-incubation of rat aorta rings in the presence of somatostatin analogs, which are preferentially sst2 specific binders: PRL-2882; PRL-2903 and PRL-2915 at micro-molar concns. significantly blocked the development of human urotensin II-induced tonic contractions. Somatostatin receptor antagonists dose-dependently inhibited human urotensin II-induced Ca²⁺ transients in rat thoracic aorta rings. These somatostatin receptor antagonists displayed moderate affinities for recombinant rat and human urotensin II receptor binding sites. The data support the suggestion that urotensin II receptor and somatostatin type 2/5 receptors display similar surface topologies and that analogs of somatostatin could provide useful lead compds. for the development of more potent urotensin II receptor antagonists.

IT 270900-25-9, Rat urotensin II

RL: BSU (Biological study, unclassified); BIOL (Biological study) (signaling pathways involved in human urotensin II-induced aorta ring contractions and inhibition by **somatostatin** receptor antagonists)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:830883 HCAPLUS

DOCUMENT NUMBER: 135:358166

TITLE: Preparation of somatostatin analogs for the treatment of cancer

INVENTOR(S): Burman, Anand C.; Prasad, Sudhanand; Mukherjee, Rama; Jaggi, Manu; Singh, Anu T.; Mathur, Archana

PATENT ASSIGNEE(S): Dabur Research Foundation, India

SOURCE: U.S., 15 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6316414	B1	20011113	US 2000-629371	20000731
PRIORITY APPLN. INFO.:			US 2000-629371	20000731

OTHER SOURCE(S): MARPAT 135:358166

AB Peptides X-D-Phe-Cys-Tyr-D-Trp-Al-A2-A3-Thr-NH₂ [X is Ac or straight, branched, or cyclic alkanoyl group of 3-18 carbon atoms, or is deleted; A1 is Orn or Lys; A2 is .alpha.-aminoisobutyric acid (Aib), .alpha.,.alpha.-diethyl- or -dipropylglycine (Deg or Dpg) or 1-aminocyclopentanecarboxylic acid (Ac5c); A3 is penicillamine (Pen) or

Cys or a hydrolyzable carboxy protecting group] or their pharmaceutically acceptable salts were prepd. for the treatment and prevention of cancer. Thus, H-D-Phe-Cys-Tyr-D-Trp-Orn-Deg-Pen-Thr-NH₂ was prepd. by the solid-phase method using a Rink Amide resin and showed significant antitumor activity on human colon adenocarcinoma xenografts (57.1% inhibition after 21 days).

IT 371242-05-6P 371242-06-7P 371242-07-8P

371242-10-3P 371242-11-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of **somatostatin** analogs for the treatment of cancer)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:827035 HCAPLUS

DOCUMENT NUMBER: 136:210716

TITLE: A bicyclic and Hsst2 selective somatostatin analogue: design, synthesis, conformational analysis and binding

AUTHOR(S): Falb, Eliezer; Salitra, Yoseph; Yechezkel, Tamar; Bracha, Moshe; Litman, Pninit; Olender, Roberto; Rosenfeld, Rakefet; Senderowitz, Hanoach; Jiang, Shaokai; Goodman, Murray

CORPORATE SOURCE: Peptor Ltd., Rehovot, 76326, Israel

SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(12), 3255-3264

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A backbone bridged and disulfide bridged bicyclic somatostatin analog, compd. 1 (PTR-3205), was designed and synthesized by solid-phase methodol. The binding of compd. 1 to the five different somatostatin receptors, expressed in CHO or COS-7 cells, indicate a high degree of selectivity towards hsstr2. The three-dimensional structure of this compd. has been detd. in DMSO-d₆ and in water by 1H NMR and by mol. dynamics simulations. Similar backbone conformations were obsd. in both solvents. The authors have established direct evidence that the backbone of this bicyclic somatostatin analog assumes a 'folded' conformation in soln., where the lactam ring extends roughly in the plane of the .beta.-turn. The pharmacophoric region Phe-(d)-Trp-Lys-Thr of compd. 1 is in accord with that of both the Veber compd. L-363,301 (Merck) and sandostatin. The authors believe that the enhanced selectivity towards the hsst2 receptor, in comparison with other analogs, is due to its large hydrophobic region, composed of the lactam ring and the Phe side chains at positions 1 and 8.

IT 401912-42-3DP, resin bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(bicyclic and hsst2 selective **somatostatin** analog: design, synthesis, conformational anal. and binding)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:614047 HCAPLUS

DOCUMENT NUMBER: 135:190390

TITLE: Antisense oligonucleotide conjugates with somatostatin analogs for treatment of tumors associated with high leves of the somatostatin receptor

INVENTOR(S): Eisenhut, Michael; Mier, Walter; Eritia, Ramon; Haberkorn, Uwe

PATENT ASSIGNEE(S): Deutsches Krebsforschungszentrum Stiftung des

SOURCE: Oeffentlichen Rechts, Germany
 Ger. Offen., 16 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10006572	A1	20010823	DE 2000-10006572	20000214
EP 1129725	A2	20010905	EP 2001-103466	20010214
EP 1129725	A3	20030122		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO

US 2001029035	A1	20011011	US 2001-781980	20010214
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PRIORITY APPLN. INFO.:	DE 2000-10006572 A	20000214
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AB The present invention concerns an oligonucleotide conjugate between an antisense DNA to an essential gene and a somatostatin analog. The present invention concerns also this oligonucleotide conjugate contg. drug, preferably to the therapy of tumors, with which the somatostatin receptor (SSTR) is over-expressed. The antisense DNA, which may contain base analogs or a modified backbone, is preferably directed against the bcl-2 oncogene. Prepn. of octreotide analogs of somatostatin and their conjugation with antisense oligonucleotides is demonstrated.

IT 356534-86-6

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (prepn. and reactions of; antisense oligonucleotide conjugates with **somatostatin** analogs for treatment of tumors assocd. with high leves of **somatostatin** receptor)

IT 356544-18-8

RL: PRP (Properties)
 (unclaimed sequence; antisense oligonucleotide conjugates with **somatostatin** analogs for treatment of tumors assocd. with high leves of the **somatostatin** receptor)

L8 ANSWER 14 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:894630 HCAPLUS

DOCUMENT NUMBER: 134:141903

TITLE: Identification and exploitation of structural foci that influence conformational mobility in somatostatin agonists and antagonists

AUTHOR(S): Morgan, Barry; Anderson, Warren; Coy, David; Culler, Michael; MacArthur, Malcolm; Mierke, Dale; Pellegrini, Maria; Piserchio, Andrea; Allee, Dean Sadat; Taylor, John

CORPORATE SOURCE: Biomeasure, Inc., Milford, MA, 01757, USA

SOURCE: Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 245-247. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Kluwer Academic Publishers: Dordrecht, Neth.
 CODEN: 69ATHX

DOCUMENT TYPE: Conference

LANGUAGE: English

AB The somatostatin (ss) agonist BIM-23023, and the recently described somatostatin antagonist BIM-23454, have modest selectivity for hSSTR2 and the authors were interested in exploring the relationship between structure and function with respect to affinity for, and efficacy at alternative somatostatin receptor subtypes. The authors carried out a retrospective anal. on structural data from the Cambridge crystallog. database (CCD), and the Protein Database (PDB) for peptides contg. a

CXXXXC fragment. The authors have also carried out structural studies using NMR methods on BIM-23023 and 23454 in both DMSO, and water contg. dodecylphosphocholine (DPC), and compared these structures to those obtained by crystallog. methods. The authors found that peptides contg. a CXXXXC sequence adopt a closely related series of "helix" conformations in the crystal state, and have found by NMR methods that this conformation is also adopted by SS agonists in aq. DPC media. The authors hypothesize that this event "primes" the peptide in a conformation appropriate for receptor binding. The authors find that an SS antagonist exists in multiple conformational states in DPC, and have shown that modification at the i+3 position of the .beta.-II' turn of this analog can reverse hSSTR2/5 selectivity and restore efficacy. The conformational basis for this reversal of selectivity and restoration of agonist character is currently under investigation.

IT 243470-86-2, BIM 23454

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(identification and exploitation of structural foci that influence conformational mobility in somatostatin agonists and antagonists)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:741964 HCAPLUS

DOCUMENT NUMBER: 133:319295

TITLE: Short-chain peptide dye conjugates used as contrast agents for optical diagnostics

INVENTOR(S): Licha, Kai; Becker, Andreas; Semmler, Wolfhard; Wiedenmann, Bertram; Hessenius, Carsten; Volkmer-Engert, Rudolf; Schneider-Mergener, Jens; Bhargava, Sarah

PATENT ASSIGNEE(S): Institut fur Diagnostikforschung G.m.b.H. an der Freien Universitat Berlin, Germany

SOURCE: PCT Int. Appl., 110 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061194	A2	20001019	WO 2000-EP2697	20000328
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
DE 19917713	A1	20001019	DE 1999-19917713	19990409
BR 2000009658	A	20020115	BR 2000-9658	20000328
EP 1176987	A2	20020206	EP 2000-922560	20000328
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2002541219	T2	20021203	JP 2000-610526	20000328
EE 200100521	A	20021216	EE 2001-521	20000328
EP 1281405	A2	20030205	EP 2002-90268	20000328
EP 1281405	A3	20030212		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			

IE, FI, CY
 NO 2001004911 A 20011206 NO 2001-4911 20011009
 PRIORITY APPLN. INFO.: DE 1999-19917713 A 19990409
 EP 2000-922560 A3 20000328
 WO 2000-EP2697 W 20000328

OTHER SOURCE(S): MARPAT 133:319295

AB The invention relates to compds. which are used for diagnosing tumors comprised of conjugates of dyes having short-chain peptides that are derived from the vasoactive intestinal peptide, from somatostatin or from neurotensin. The invention also relates to the use of these compds. as optical diagnostic agents and to diagnostic products contg. these compds. Peptide-polymethine dye conjugates are described with the general formula Al-(X)m-A2; where X = .alpha., .beta., .gamma. amino acid with D or L conf.; m = 5-30 linear or disulfide bridge contg.; Al = H, acyl, alkyl up to C10, C1-3 carboxyl, or OH substituted, polyethylene oxyde, or polyemethyne dye with adsorption at 380 - 1200 nm; A2 = hydroxy, amino, or polymethyne dye with adsorption at 380 - 1200 nm; at least one of Al and A2 is a polymethyne dye.

IT 302794-47-4D, conjugate with sodium indocyanine derivs.

302794-48-5D, conjugate with sodium indocyanine derivs.

RL: RCT (Reactant); RACT (Reactant or reagent)

(somatostatin peptide; short-chain peptide dye conjugates used as contrast agents for optical diagnostics)

L8 ANSWER 16 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:708453 HCAPLUS

DOCUMENT NUMBER: 131:310841

TITLE: Procedure for obtaining the somatostatin analog octreotide

INVENTOR(S): Clemente Rodriguez, Francisco Javier; Ponsati Obiols, Berta; Jodas Farres, Gemma; Canas Poblet, Marc

PATENT ASSIGNEE(S): Lipotec, S.A., Spain

SOURCE: Eur. Pat. Appl., 11 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 953577	A1	19991103	EP 1999-500012	19990127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
ES 2144357	A1	20000601	ES 1998-162	19980129
ES 2144357	B1	20001216		
US 6346601	B1	20020212	US 1999-240145	19990129

PRIORITY APPLN. INFO.: ES 1998-162 A 19980129

AB Octreotide was obtained by solid phase synthesis on polymer supports using protective groups of the Fmoc/tBu type. Thus, Boc-D-Phe-Cys(Trt)-Phe-D-Trp-Lys(Boc)Thr(tBu)-Cys(Trt)-OH was prepd. by the solid phase method and cyclized using iodine and coupled with threoninol (either order) and then deprotected using TFA to afford octreotide in >40% yield and >99% purity.

IT 247590-52-9DP, resin-bound 247590-52-9P

247590-55-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of octreotide, a somatostatin analog)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:670109 HCAPLUS

DOCUMENT NUMBER: 131:295567
 TITLE: Inhibition of Helicobacter pylori proliferation
 INVENTOR(S): Kaneko, Hiroshi; Mitsuma, Terunori; Yamashita, Koichi;
 Morgan, Barry
 PATENT ASSIGNEE(S): Biomeasure, Inc., USA
 SOURCE: U.S., 19 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5968903	A	19991019	US 1998-74117	19980507
WO 9956769	A2	19991111	WO 1999-US10058	19990506
WO 9956769	A3	20001109		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9939754	A1	19991123	AU 1999-39754	19990506
EP 1075273	A2	20010214	EP 1999-922851	19990506
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI			
JP 2002513769	T2	20020514	JP 2000-546793	19990506
NO 2000005588	A	20010105	NO 2000-5588	20001106
PRIORITY APPLN. INFO.:			US 1998-74117	A1 19980507
			WO 1999-US10058	W 19990506

OTHER SOURCE(S): MARPAT 131:295567

AB The present invention is directed to a method of using somatostatin or a somatostatin agonist to inhibit the proliferation of Helicobacter pylori (H. pylori), which comprises administering to a patient in need thereof an effective amt. of said somatostatin or somatostatin agonist. Preferably, a somatostatin sub-type receptor 2 (SSTR-2) selective somatostatin agonist is administered in a method of this invention. The inhibition of H. pylori proliferation is useful in treating various gastroduodenal diseases such as peptic ulcers, gastric cancer and gastric lymphoma.

IT 95833-38-8 103222-03-3 103548-90-9
 109791-07-3 109791-08-4 110786-64-6
 113294-82-9 113294-83-0 113294-84-1
 113294-89-6 120796-15-8 145758-77-6
 150957-55-4 152510-40-2 173484-74-7
 204387-62-2 204387-63-3 204387-64-4
 204387-65-5 204387-66-6 204387-67-7
 204387-68-8 204387-69-9 204387-70-2
 204387-71-3 204387-72-4 204387-73-5
 204387-74-6 204387-75-7 204387-76-8
 204387-77-9 204387-78-0 204387-79-1
 204387-80-4 204387-81-5 204387-82-6
 204387-83-7 204387-84-8 204387-85-9
 204387-86-0 204387-87-1 204387-88-2
 204387-89-3 204387-90-6 204387-91-7
 204387-96-2 204387-97-3 204388-13-6
 204388-14-7 204518-70-7 204518-71-8
 205652-45-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of Helicobacter pylori proliferation with
somatostatin or a somatostatin agonist)

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:562089 HCAPLUS

DOCUMENT NUMBER: 131:331722

TITLE: Novel Lipoamino Acid- and Liposaccharide-Based System
for Peptide Delivery: Application for Oral
Administration of Tumor-Selective Somatostatin Analogs

AUTHOR(S): Toth, Istvan; Malkinson, John P.; Flinn, Nicholas S.;
Drouillat, Bruno; Horvath, Aniko; Erchegeyi, Judith;
Idel, Miklos; Venetianer, Aniko; Artursson, Per;
Lazorova, Lucia; Szende, Bela; Keri, Gyoergy

CORPORATE SOURCE: Department of Pharmaceutical and Biological Chemistry
The School of Pharmacy, University of London, London,
WC1N 1AX, UK

SOURCE: Journal of Medicinal Chemistry (1999), 42(19),
4010-4013

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lipoamino acid and liposaccharide conjugates of somatostatin analog TT-232
were synthesized to modify the physicochem. properties of the parent
peptide. The relative position, the no., and the nature of the lipid
and/or saccharide moieties were varied. Expts. in vitro clearly showed
that many compds. modified at the N- and/or C-terminus with lipid or sugar
moieties retained the biol. activity of the parent compd. An interesting
construct was synthesized contg. lipid and sugar units at opposite ends of
the somatostatin analog, so that the entire mol. could be considered as an
amphipathic surfactant.

IT 244303-43-3P 250132-09-3P 250132-10-6P
250132-11-7P 250132-13-9P 250132-14-0P
250132-15-1P 250132-16-2P 250132-17-3P
250132-18-4P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); BSU (Biological study, unclassified); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(lipoamino acid- and liposaccharide-based system for application for
oral administration of tumor-selective somatostatin analogs)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:458425 HCAPLUS

DOCUMENT NUMBER: 132:148528

TITLE: Technetium-99m somatostatin analogues: effect of
labelling methods and peptide sequence

AUTHOR(S): Decristoforo, Clemens; Mather, Stephen J.

CORPORATE SOURCE: Nuclear Medicine Research Laboratory, St.
Bartholomew's Hospital, West Smithfield, London, EC1A
7BE, UK

SOURCE: European Journal of Nuclear Medicine (1999), 26(8),
869-876

CODEN: EJNMD9; ISSN: 0340-6997

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In this paper the preclin. evaluation of the somatostatin analog RC160
labeled with technetium-99m using bifunctional chelators (BFCs) based on
the hydrazinonicotinamide (HYNIC) and N3S system is described and a

comparison made with [Tyr3]-octreotide (TOC). Conjugates of both peptides with HYNIC, and of RC160 with benzoyl-MAG3 and an N3S-adipate deriv. were prepd. and radiolabelling performed at high specific activities using tricine, tricine/nicotinic acid and ethylenediamine-N,N'-diacetic acid (EDDA) as co-ligands for HYNIC conjugates. All conjugates and 99mTc-labeled peptides showed preserved binding affinity for the somatostatin receptor (IC50, Kd<5 nM). The biodistribution was markedly dependent on the BFC and co-ligand used, with the amidothiol ligands showing a greater degree of hepatobiliary clearance, the HYNIC/tricine complex higher blood levels and the HYNIC/EDDA complex the highest level of renal excretion and lowest blood levels. All peptide conjugates showed receptor-mediated uptake in tumor xenografts, but tumor uptake was significantly lower for the 99mTc-RC160 derivs. compared with 99mTc-EDDA/HYNIC-[Tyr3]-octreotide (0.2%-3.5%ID/g vs 9.7%ID/g) and correlated well with the reduced internalization rate for RC160 derivs. Our results show that the selection of the labeling approach as well as the right choice of the peptide structure are crucial for labeling peptides with 99mTc to achieve complexes with favorable biodistribution. Despite the relatively low tumor uptake compared with 99mTc-EDDA/HYNIC-[Tyr3]-octreotide, 99mTc-RC160 could play a role in imaging tumors that do not bind octreotide derivs.

IT 257943-18-3 257943-18-3D, technetium-99 complex

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(technetium-99m complexes with somatostatin analogs: prepn., biodistribution and tumor uptake)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 20 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:396776 HCAPLUS

DOCUMENT NUMBER: 131:248135

TITLE: A novel lipoamino acid based system for peptide delivery: application for administering tumor selective somatostatin analogues

AUTHOR(S): Flinn, Nicholas S.; Erchegeyi, Judit; Horvath, Aniko; Keri, Gyorgy; Toth, Istvan

CORPORATE SOURCE: Dept. Of Pharmaceutical and Biological Chemistry, The School of Pharmacy, University of London, London, WC1N 1AX, UK

SOURCE: Peptides: Frontiers of Peptide Science, Proceedings of the American Peptide Symposium, 15th, Nashville, June 14-19, 1997 (1999), Meeting Date 1997, 843-844. Editor(s): Tam, James P.; Kaumaya, Pravin T. P. Kluwer: Dordrecht, Neth. CODEN: 67UCAR

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Somatostatin analogs were prepd. which were extended on their N-terminus with either one or two lipoamino acids having side chains of varying lengths. The compds. were used as antitumor agents in either their oxidized (cyclic) form or as the linear (Acm-protected) derivs. Cyclizations were performed off-resin using 20-30 equiv of iodine in 95% acetic acid. The tumor cell lines used were HT29 (colonic), PC3 (prostatic), SW620 (colonic) and A2068 (melanoma). Various selectivities in antitumor activity are reported for 5 analogs.

IT 244303-42-2 244303-43-3

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(lipoamino acid-based system for peptide delivery: application for administering tumor selective somatostatin analogs)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:396636 HCAPLUS
 DOCUMENT NUMBER: 131:208607
 TITLE: Somatostatin receptor antagonists based on a mixed
 neuromedin B antagonist/somatostatin agonist
 AUTHOR(S): Coy, David H.; Jain, Rahul; Murphy, William A.;
 Rossowski, Wojciech J.; Fuselier, Joseph; Taylor, John
 E.
 CORPORATE SOURCE: Peptide Research Laboratories, Department of Medicine,
 Tulane University Medical Center, New Orleans, LA,
 70112, USA
 SOURCE: Peptides: Frontiers of Peptide Science, Proceedings of
 the American Peptide Symposium, 15th, Nashville, June
 14-19, 1997 (1999), Meeting Date 1997, 526-529.
 Editor(s): Tam, James P.; Kaumaya, Pravin T. P.
 Kluwer: Dordrecht, Neth.
 CODEN: 67UCAR
 DOCUMENT TYPE: Conference
 LANGUAGE: English

AB The somatostatin-antagonizing activities are reported for 19 analogs of
 D-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Nal-NH₂. The high potencies in this type
 of type-2 receptor-specific somatostatin antagonists reside in the use of
 optimized arom. amino acid structures in positions 1 and 8. It was
 thought that the ability of these side-chains to form .pi.-.pi. complexes
 might offer an explanation for these results. However, mol. modeling
 studies in progress on these octapeptides suggest little possibility that
 this occurs. The D-Cys₂ residue appears to force rotation of the position
 1 side chains so that they protrude in the opposite direction to agonist
 side-chains with the remainder of the mol. being little changed. This may
 be the reason for their antagonist properties.

IT 243470-72-6 243470-73-7 243470-74-8
 243470-75-9 243470-76-0 243470-77-1
 243470-78-2 243470-79-3 243470-80-6
 243470-81-7 243470-82-8 243470-83-9
 243470-84-0 243470-85-1 243470-86-2
 243470-87-3 243470-88-4 243470-89-5
 243470-90-8

RL: BAC (Biological activity or effector, except adverse); BPR (Biological
 process); BSU (Biological study, unclassified); PRP (Properties); THU
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (somatostatin receptor antagonists based on a mixed
 neuromedin B antagonist/somatostatin agonist)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 22 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:396523 HCAPLUS
 DOCUMENT NUMBER: 131:209383
 TITLE: Isolation, characterization, and synthesis of a
 trisulfide related to the somatostatin analog
 Lanreotide
 AUTHOR(S): Chen, Lin; Skinner, Steven R.; Gordon, Thomas D.;
 Taylor, John E.; Barany, George; Morgan, Barry A.
 CORPORATE SOURCE: Dept. of Chemistry, University of Minnesota,
 Minneapolis, MN, 55455, USA
 SOURCE: Peptides: Frontiers of Peptide Science, Proceedings of
 the American Peptide Symposium, 15th, Nashville, June
 14-19, 1997 (1999), Meeting Date 1997, 275-276.
 Editor(s): Tam, James P.; Kaumaya, Pravin T. P.
 Kluwer: Dordrecht, Neth.
 CODEN: 67UCAR

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Lanreotide trisulfide, a side-product isolated from Lanreotide crude product, was synthesized by a directed reaction of a nucleophilic .beta.-thiol from an internal cysteine residue onto an S-[(N'-methyl-N-phenylcarbamoyl)disulfanyl]-protected cysteine residue, isolated by HPLC, and characterized by electrospray MS. The pure trisulfide was tested for affinity for human somatostatin receptor subtypes hSSTR1-5. The trisulfide has an affinity profile similar to Lanreotide but was more selective towards the hSSTR2 subtype due to a decreased Ki at the hSSTR5 subtype.

IT 243470-24-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(Lanreotide trisulfide synthesis and **somatostatin** receptor binding activity)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:326492 HCAPLUS

DOCUMENT NUMBER: 131:248216

TITLE: Labeling peptides with rhenium-188

AUTHOR(S): Melendez-Alafort, L.; Ferro-Flores, G.; Arteaga-Murphy, C.; Pedraza-Lopez, M.; Gonzalez-Zavala, M. A.; Tendilla, J. I.; Garcia-Salinas, L.

CORPORATE SOURCE: Instituto Nacional de Nutricion, Salvador Zubiran, Mex.

SOURCE: International Journal of Pharmaceutics (1999), 182(2), 165-172

CODEN: IJPHDE; ISSN: 0378-5173

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A direct labeling technique via EHDP for the prepn. of 188Re-somatostatin analog peptide .beta.-(2-naphthyl)-D-Ala-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-amide complex was developed. The influence of reaction conditions such as pH, temp., weak ligand concn. and stannous chloride concn. were investigated. Methods of anal. were also established permitting identification of radiochem. impurities which may be present in the radiopharmaceutical soln. Results showed that under the procedure reported herein 188Re-peptide complex can be prepd. with a radiochem. purity of 90% and a specific activity up to 1.8 GBq mg-1 without radiolytic degrdn. of the product.

IT 113294-82-9DP, rhenium-188 complex

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(**somatostatin** analog peptide labeled with rhenium-188)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:200848 HCAPLUS

DOCUMENT NUMBER: 130:312081

TITLE: Synthesis and characterization of multiply-tyrosinated, multiply-iodinated somatostatin analogs

AUTHOR(S): Woltering, E. A.; O'Dorisio, M. S.; Murphy, W. A.; Chen, F.; Drouant, G. J.; Espenan, G. D.; Fisher, D. R.; Sharma, C.; Diaco, D. S.; Maloney, T. M.; Fuselier, J. A.; Nelson, J. A.; O'Dorisio, T. M.; Coy, D. H.

CORPORATE SOURCE: Department of Surgery, Section of Surgical

Endocrinology and the Stanley S. Scott Cancer Center,
Louisiana State University Medical Center, New
Orleans, LA, 70112, USA
SOURCE: Journal of Peptide Research (1999), 53(2), 201-213
CODEN: JPERFA; ISSN: 1397-002X
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Radio-labeled somatostatin analogs have recently gained popularity as agents useful in intra-operative tumor localization, external scintigraphy and in situ radiotherapy. We have synthesized and characterized a series of novel N-terminally extended multiply-tyrosinated somatostatin analogs that possess high binding affinity for somatostatin receptors, exhibit biol. activity comparable to the native peptide and retain these characteristics after iodination. These analogs can be radio-iodinated to high specific activities. Following radio-iodination, these analogs exhibit minimal radiolysis and may be clin. useful for tumor localization, scanning and therapy.

IT 223659-56-1P 223659-57-2P 223659-58-3P
223659-59-4P 223659-60-7P 223659-61-8P
223659-62-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and characterization of multiply-tyrosinated multiply-iodinated **somatostatin** analogs)

IT 223659-57-2DP, radio-iodinated 223659-58-3DP,
radio-iodinated 223659-59-4DP, radio-iodinated
223659-60-7DP, radio-iodinated

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and characterization of multiply-tyrosinated multiply-iodinated **somatostatin** analogs)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:66786 HCAPLUS

DOCUMENT NUMBER: 130:322390

TITLE: Internalization of [DOTA.degree., 125I-Tyr3]octreotide by somatostatin receptor-positive cells in vitro and in vivo: implications for somatostatin receptor-targeted radioguided surgery

AUTHOR(S): Hofland, Leo J.; Breeman, Wout A. P.; Krenning, Eric P.; de Jong, Marion; Waaijers, Marlijn; van Koetsveld, Peter M.; Macke, Helmut R.; Lamberts, Steven W. J.
CORPORATE SOURCE: Department of Internal Medicine III, Erasmus University, Rotterdam, Neth.

SOURCE: Proceedings of the Association of American Physicians (1999), 111(1), 63-69
CODEN: PAAPFD; ISSN: 1081-650X

PUBLISHER: Blackwell Science, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We compared internalization of three radioiodinated octreotide (OCT) somatostatin (SS) analogs-[125I-Tyr3]OCT, [DTPA.degree.,125I-Tyr3]OCT, and [DOTA.degree.,125I-Tyr3]OCT-by somatostatin receptor (SSR)-pos. mouse AtT20 pituitary tumor cells and human insulinoma cells. The three SS analogs were internalized in a specific, time-dependent manner. Internalization was significantly inhibited by pertussis toxin (100 .mu.g/l) by 38%, 43%, and 31%, and by an inhibitor of receptor-mediated

endocytosis (Ph arsine oxide; 10 .mu.M) by 98%, 94%, and 92%, resp. Binding affinities of the three radioligands were comparable (0.2, 0.2, and 0.3 nM, resp.). However, [DOTA.degree.,125I-Tyr3]OCT was internalized in a five-fold higher amt. in comparison with the two other radioligands. A comparably high uptake of [DOTA.degree.,125I-Tyr3]OCT was found in SSR-pos. organs (pituitary, pancreas, and adrenals) in vivo in rats (a ten-fold, five-fold, and eight-fold higher uptake 4 h post injection, resp., compared with the two other radioligands). This resulted in very high target-background ratios for [DOTA.degree.,125I-Tyr3]OCT 4 h post injection amounting to 274, 566, and 623 in the pituitary, adrenals, and pancreas, resp. Both in vivo and in vitro there was a rapid dissocn. of radioactivity from the SSR-pos. cells. Main conclusions are that: (1) coupling of chelating groups like DTPA or DOTA to the SS analog [Tyr3]OCT does not prevent the internalization of OCT after binding to SSRs; (2) [DOTA.degree.,125I-Tyr3]OCT is internalized in a significantly higher amt. by AtT20 and human insulinoma cells and in vivo in rats in SSR-pos. organs, in comparison with [DTPA.degree.,125I-Tyr3]OCT and [125I-Tyr3]OCT; and (3) the very high target-background ratios in vivo make radioiodinated [DOTA.degree.,Tyr3]OCT a very suitable ligand for SSR-targeted radioguided surgery of SSR-pos. human neuroendocrine tumors.

IT 204318-21-8

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(internalization of radioiodinated octreotide **somatostatin** analogs by **somatostatin** receptor-pos. cells in vitro and in vivo)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:788734 HCAPLUS

DOCUMENT NUMBER: 130:47494

TITLE: Pure somatostatin antagonist and methods of use thereof

INVENTOR(S): Bass, Roy Tyson; Buckwalter, Brian Lee; Hadcock, John Richard; Patel, Bomi Pilloo; Chiarello, John Francis

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: U.S., 8 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5846934	A	19981208	US 1997-801374	19970219
PRIORITY APPLN. INFO.:			US 1997-801374	19970219

OTHER SOURCE(S): MARPAT 130:47494

AB Somatostatin antagonist peptides that are selective for subtypes SSTR2 and SSTR5 are described. The present invention also relates to these peptides with increasing the release of growth hormone, insulin, and glucagon in mammals, and a method for the enhancement of growth.

IT 195520-39-9P 195520-40-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptidic **somatostatin** antagonists and effects on growth hormone, insulin and glucagon release)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:764305 HCAPLUS
 DOCUMENT NUMBER: 130:20992
 TITLE: Somatostatin and somatostatin agonists for treating insulin insensitivity and Syndrome X
 INVENTOR(S): Cawthorne, Michael Anthony; Liu, Yong-Ling; Sennitt, Matthew V.
 PATENT ASSIGNEE(S): Societe De Conseils De Recherches Et D'Applications Scientifiques S.A. (S.C., Fr.
 SOURCE: PCT Int. Appl., 55 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851332	A1	19981119	WO 1998-EP3000	19980513
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9880198	A1	19981208	AU 1998-80198	19980513
EP 980253	A1	20000223	EP 1998-928308	19980513
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1997-854943	19970513
			WO 1998-EP3000	19980513
OTHER SOURCE(S): MARPAT 130:20992				
AB The present invention relates to a method of treating insulin resistance or Syndrome X. The method includes the step of administering a therapeutically effective amt. of a somatostatin or a somatostatin agonist to said patient. The invention also includes pharmaceutical compns. comprising a somatostatin or somatostatin agonist and the use of such products in the prepn. of such compns.				
IT 113294-84-1 204388-13-6 204388-14-7 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (somatostatin and somatostatin agonists for treating insulin insensitivity and Syndrome X)				
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT				

L8 ANSWER 28 OF 48 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1998:764304 HCAPLUS
 DOCUMENT NUMBER: 130:20991
 TITLE: Somatostatin and somatostatin agonists for decreasing body weight
 INVENTOR(S): Cawthorne, Michael Anthony; Liu, Yong-Ling; Sennitt, Matthew V.
 PATENT ASSIGNEE(S): Societe De Conseils De Recherches Et D'Applications Scientifiques S.A. (S.C., Fr.
 SOURCE: PCT Int. Appl., 41 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851331	A1	19981119	WO 1998-EP2999	19980513
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9876550	A1	19981208	AU 1998-76550	19980513
EP 981363	A1	20000301	EP 1998-924317	19980513
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1997-854941	19970513
			WO 1998-EP2999	19980513
OTHER SOURCE(S): MARPAT 130:20991				
AB The present invention relates to a method of decreasing body wt. in a patient. The method includes the step of administering a therapeutically effective amt. of a somatostatin or a somatostatin agonist to said patient. A pharmaceutical/cosmetic compn. comprises the somatostatin or somatostatin agonist. Such products are used to prep. such compns. for the redn. of body wt. in a human or mammalian animal.				
IT 113294-84-1 204388-13-6 204388-14-7 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (somatostatin and somatostatin agonists for decreasing body wt.)				
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT				
L8 ANSWER 29 OF 48 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1998:163467 HCAPLUS DOCUMENT NUMBER: 128:226683 TITLE: Method of inhibiting fibrosis with a somatostatin agonist INVENTOR(S): Culler, Michael D.; Kasprzyk, Philip G. PATENT ASSIGNEE(S): Biomeasure Incorporated, USA; Culler, Michael D.; Kasprzyk, Philip G. SOURCE: PCT Int. Appl., 61 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 3 PATENT INFORMATION:				

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808529	A1	19980305	WO 1997-US14154	19970827
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9741490	A1	19980319	AU 1997-41490	19970827
AU 726731	B2	20001116		
EP 938328	A1	19990901	EP 1997-939392	19970827

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

CN 1229357	A	19990922	CN 1997-197671	19970827
JP 2001500483	T2	20010116	JP 1998-511678	19970827
ZA 9707783	A	19990301	ZA 1997-7783	19970829
US 6268342	B1	20010731	US 1999-254097	19990510

PRIORITY APPLN. INFO.: US 1996-705790 A2 19960830
WO 1997-US14154 W 19970827

OTHER SOURCE(S): MARPAT 128:226683

AB The present invention relates to a method of inhibiting fibrosis in a patient. The method comprises administering a therapeutically effective amt. of a somatostatin, a somatostatin agonist or a pharmaceutically acceptable salt thereof to said patient.

IT 95833-38-8 103222-03-3 103548-90-9
109791-07-3 109791-08-4 110786-64-6
113294-82-9 113294-83-0 113294-84-1
113294-89-6 120796-15-8 145758-77-6
150957-55-4 150957-56-5 150996-95-5
152510-40-2 173484-74-7 204387-62-2
204387-63-3 204387-64-4 204387-65-5
204387-66-6 204387-67-7 204387-68-8
204387-69-9 204387-70-2 204387-71-3
204387-72-4 204387-73-5 204387-74-6
204387-75-7 204387-76-8 204387-77-9
204387-78-0 204387-79-1 204387-80-4
204387-81-5 204387-82-6 204387-83-7
204387-84-8 204387-85-9 204387-86-0
204387-87-1 204387-88-2 204387-89-3
204387-90-6 204387-91-7 204387-96-2
204387-97-3 204388-13-6 204388-14-7
204518-70-7 204518-71-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(method of inhibiting fibrosis with a **somatostatin** agonist)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 30 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:133534 HCAPLUS

DOCUMENT NUMBER: 128:162873

TITLE: Cationic liposome:DNA complex vehicles encoding anti-angiogenic peptides for use in gene therapy

INVENTOR(S): Mixson, Archibald James

PATENT ASSIGNEE(S): Mixson, Archibald James, USA

SOURCE: Eur. Pat. Appl., 47 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
EP 819758	A2	19980121	EP 1997-112154	19970716
EP 819758	A3	19980204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6080728	A	20000627	US 1997-985526	19971205
JP 11187886	A2	19990713	JP 1998-201996	19980716
US 2002151516	A1	20021017	US 2001-36869	20011129

PRIORITY APPLN. INFO.: US 1996-680845 A 19960716
EP 1997-112154 A 19970716

US 1997-985526 A 19971205
US 2000-500838 B1 20000210

AB Cationic vehicles:DNA complexes comprising DNA encoding an anti-angiogenic peptide or DNA encoding a tumor suppressor protein and DNA encoding an anti-angiogenic peptide, as well as their use in gene therapy, are disclosed. The liposomal components may comprise 1,2-dioleoyl-sn-glycero-3-ethylphosphocholine, 1,2-dimyristoyl-sn-glycero-3-ethylphosphocholine, and 2,3-dioleoyloxy(propyl-N,N,N-trimethylammonium chloride), optionally in combination with polyethylene glycol and a targeted ligand such as Arg-Gly-Asp, ferritin, or antibodies targeted toward HER2. DNA is prep'd. encoding anti-angiogenic peptide fragments of thrombospondin I, fibronectin, laminin, platelet factor 4, angiostatin, and prolactin, as well as concatemers of these fragments. Tumor suppressor protein genes include p53, p21, or Rb. Thus, liposome:DNA vectors encoding p53 in combination with a thrombospondin I fragment reduced tumors more effectively than p53 alone. The cationic polymer allows superior transfection of endothelial cells; Superfect is a better transfection agent than cationic liposomes for many different cell lines.

IT 202645-54-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**somatostatin** fragment; cationic liposome:DNA complex
vehicles encoding anti-angiogenic peptides for use in gene therapy)

L8 ANSWER 31 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:95370 HCAPLUS

DOCUMENT NUMBER: 128:215052

TITLE: Pre-clinical comparison of [DTPA0] octreotide, [DTPA0,Tyr3] octreotide and [DOTA0,Tyr3] octreotide as carriers for somatostatin receptor-targeted scintigraphy and radionuclide therapy

AUTHOR(S): De Jong, Marion; Bakker, Willem H.; Breeman, Wout A. P.; Bernard, Bert F.; Hofland, Leo J.; Visser, Theo J.; Srinivasan, Ananth; Schmidt, Michelle; Behe, Martin; Macke, Helmut R.; Krenning, Eric P.

CORPORATE SOURCE: Department of Nuclear Medicine, University. Hospital Dijkzigt, Rotterdam, 3015 GD, Neth.

SOURCE: International Journal of Cancer (1998), 75(3), 406-411
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have evaluated the potential usefulness of radiolabeled [DTPA0,Tyr3]octreotide and [DOTA.degree.,Tyr3]octreotide as radiopharmaceuticals for somatostatin receptor-targeted scintigraphy and radiotherapy. In vitro somatostatin receptor binding and in vivo metab. in rats of the compds. were investigated in comparison with [111In-DTPA.degree.] octreotide. Comparing different peptide-chelator constructs, [DTPA0,Tyr3]octreotide and [DOTA0,Tyr3]octreotide were found to have a higher affinity than [DTPA0]octreotide for subtype 2 somatostatin receptors (sst2) in mouse AtT20 pituitary tumor cell membranes (all IC50 values obtained were in the low nanomolar range). In vivo studies in CA20948 tumor-bearing Lewis rats revealed a significantly higher uptake of both 111In-labeled [DOTA0,Tyr3]octreotide and [DTPA0,Tyr3]octreotide in sst2-expressing tissues than after injection of [111In-DTPA0]octreotide, showing that substitution of Tyr for Phe at position 3 in octreotide results in an increased affinity for its receptor and in a higher target tissue uptake. Uptake of 111In-labeled [DTPA0]octreotide, [DTPA0,Tyr3]octreotide and [DOTA0,Tyr3]octreotide in pituitary, pancreas, adrenals and tumor was decreased to less than 7% of control by pre-treatment with 0.5 mg unlabeled octreotide/rat, indicating specific binding to sst2. Comparing different radionuclides,

[90Y-DOTA0,Tyr3]octreotide had the highest uptake in sst2-pos. organs, followed by the [111In-DOTA0,Tyr3]octreotide, whereas [DOTA0,125I-Tyr3]octreotide uptake was low compared to that of the other radiopharmaceuticals, when measured 24 h after injection. Renal uptake of 111In-labeled [DTPA0]octreotide, [DTPA0,Tyr3]octreotide and [DOTA0,Tyr3]octreotide was reduced over 50% by an i.v. injection of 400 mg/kg D-lysine, whereas radioactivity in blood, pancreas and adrenals was not affected.

IT 204318-21-8

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pre-clin. comparison of [DTPA0] octreotide, [DTPA0,Tyr3] octreotide and [DOTA0,Tyr3] octreotide as carriers for **somatostatin** receptor-targeted scintigraphy and radionuclide therapy)

L8 ANSWER 32 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:589211 HCAPLUS

DOCUMENT NUMBER: 127:248422

TITLE: Preparation of peptide derivatives as somatostatin antagonists and measurement of their biological activities

INVENTOR(S): Bass, Roy Tyson; Buckwalter, Brian Lee; Hadcock, John Richard; Patel, Bomi Pilloo; Chiarello, John Francis

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: Eur. Pat. Appl., 19 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 791603	A2	19970827	EP 1997-301092	19970220
EP 791603	A3	19980812		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 09328499	A2	19971222	JP 1997-46968	19970217
CA 2197833	AA	19970821	CA 1997-2197833	19970218
AU 9714800	A1	19970828	AU 1997-14800	19970220
AU 721710	B2	20000713		
ZA 9701483	A	19980820	ZA 1997-1483	19970220
			US 1996-604044	A 19960220

PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 127:248422

AB Titled peptides R1R2AA1-cyclo(D-Cys-AA2-D-Trp-AA3-AA4-Cys)-AA5-NH2 [R1 = R2 = H, C1-8 alkyl, COR, CO2R where R = C1-8 alkyl, (substituted) Ph, (substituted) naphthyl; AA1 = AA2 = D- or L-arom. .alpha.-amino acid; AA3 = D- or L-Arg, Lys, Orn, Cit (Citrulline); AA4 = Val, Leu, Ile, Abu (.alpha.-aminobutyric acid), Nle, Thr, 3-(alkyl)Ser, Thr(Bzl), Ser(Bzl) with the proviso that when AA4 = Thr then AA1 = L-isomer; AA5 = D- or L-arom. .alpha.-amino acid, N-MeAla, N.alpha.-(alkyl)amino acid, Thr, Ser] were prepd. as somatostatin antagonists. H-p-NO2Phe-D-Cys-Tyr-D-Trp-Lys-Val-Cys-N.alpha.MeAla-NH2 was prepd. on a Millipore 9050 peptide synthesizer using PAL resin and std. Fmoc chem. The somatostatin antagonist activity of the above peptide in cyclized form was measured to be 3 (in a scale of 1-5 where 5 is the max. antagonist activity) in an yeast assay.

IT 195520-39-9DP, resin-bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of peptide derivs. as **somatostatin** antagonists and measurement of their biol. activities)

L8 ANSWER 33 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:194419 HCAPLUS
 DOCUMENT NUMBER: 126:248350
 TITLE: Radiolabeled somatostatin analogs in prostate cancer
 AUTHOR(S): Thakur, M. L.; Kolan, H.; Li, J.; Wiaderkiewicz, R.;
 Pallela, V. R.; Duggaraju, R.; Schally, A. V.
 CORPORATE SOURCE: DEPARTMENT OF RADIOLOGY, THOMAS JEFFERSON UNIVERSITY
 HOSPITAL, PHILADELPHIA, PA, 19107, USA
 SOURCE: Nuclear Medicine and Biology (1997), 24(1), 105-113
 CODEN: NMBIEO; ISSN: 0883-2897
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Vapreotide (RC-160), a somatostatin analog, was labeled with ^{99m}Tc by a direct method and also by using CPTA [1,4,8,11-tetraazacyclotetradecane] as a bifunctional chelating agent. The labeled compds. were evaluated in nude mice bearing exptl. human prostate cancers. In these studies, ¹¹¹In-DTPA-D-Phe-Octreotide (¹¹¹In-DTPA-octreotide) served as a std. and ^{99m}Tc-oxytocin as a receptor-nonspecific control. ^{99m}Tc-octreotide was also used. The 24 h tumor uptake of ^{99m}Tc-RC-160 was nearly 400% higher, (p < 0.05), than that of ¹¹¹In-DTPA-octreotide and diminished upon receptor blocking. In all tissues except the kidneys, the uptake of ^{99m}Tc-RC-160 was also higher than that of ¹¹¹In-DTPA-octreotide. The uptake of ^{99m}Tc-RC-160 was influenced by the amt. of peptide injected and the best tumor/muscle and tumor/blood ratios were obtained when only one .mu.g of the peptide (200 Ci/mmol) was administered.

IT **188605-37-ODP**, resin-bound **188605-39-2P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate; ^{99m}Tc-RC-160 **somatostatin** analog prepn.and
 metab. in prostate cancer for potential imaging)

L8 ANSWER 34 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:134734 HCAPLUS
 DOCUMENT NUMBER: 126:141513
 TITLE: Multi-tyrosinated somatostatin analogs, preparation thereof, and diagnostic and therapeutic use
 INVENTOR(S): Coy, David H.; Woltering, Eugene A.; O'Dorisio, M. Sue; O'Dorisio, Thomas M.; Murphy, William A.
 PATENT ASSIGNEE(S): Administrators of the Tulane Educational Fund, USA; Ohio State University Research Foundation; Louisiana State University Medical Center Foundation; Children's Hospital, Inc.
 SOURCE: PCT Int. Appl., 65 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639161	A1	19961212	WO 1996-US8437	19960603
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 5597894	A	19970128	US 1995-462223	19950605
CA 2222962	AA	19961212	CA 1996-2222962	19960603
AU 9660317	A1	19961224	AU 1996-60317	19960603
AU 709506	B2	19990902		
EP 833646	A1	19980408	EP 1996-917939	19960603

EP 833646 B1 19991201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, SE, PT, IE
JP 11507622 T2 19990706 JP 1996-501040 19960603
AT 187075 E 19991215 AT 1996-917939 19960603
ES 2140858 T3 20000301 ES 1996-917939 19960603
PRIORITY APPLN. INFO.: US 1995-462223 A 19950605
WO 1996-US8437 W 19960603

AB Disclosed are methods and compns. for the diagnosis and treatment of diseases assocd. with aberrant expression of a somatostatin receptor (e.g., cancer) or with increased prodn. of a factor regulatable by somatostatin (e.g., acromegaly). The compds. of the invention are of the general formulas (Y)n+1P, (Y)n-Ala-Y-P, or (YqXq-1)(YsXs-1)XP [P = somatostatin peptide analog binding to somatostatin receptor; Y = D-tyrosine, L-tyrosine, desaminotyrosine; n, q, s = 1-32 (q and s can be same or different); X = D-NH2-CH(CH2)mNH2-CO2H, L-NH2-CH(CH2)mNH2-CO2H (m = 1-10)]. Prepn. and radioiodination of somatostatin analog peptides of the invention are described, as are receptor binding assays and use in in vivo diagnosis and therapy of a tumor patient.

IT **186293-13-ODP**, multi-tyrosinated derivs. **186293-14-1DP**, multi-tyrosinated derivs. **186293-15-2DP**, multi-tyrosinated derivs.
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(multi-tyrosinated **somatostatin** analogs, prepn. thereof, and diagnostic and therapeutic use)

IT **186514-22-7DP**, resin-bound **186514-23-8DP**, resin-bound **186514-24-9DP**, resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(multi-tyrosinated **somatostatin** analogs, prepn. thereof, and diagnostic and therapeutic use)

L8 ANSWER 35 OF 48 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:695906 HCAPLUS
DOCUMENT NUMBER: 126:26918
TITLE: Somatostatin-based neuromedin B receptor antagonists: Dissociation of neuromedin B and somatostatin receptor binding
AUTHOR(S): Coy, D. H.; Jiang, N. -Y.; Taylor, J. E.
CORPORATE SOURCE: Medical Center, Tulane University, New Orleans, LA, 70112, USA
SOURCE: Peptides: Chemistry, Structure and Biology, Proceedings of the American Peptide Symposium, 14th, Columbus, Ohio, June 18-23, 1995 (1996), Meeting Date 1995, 344-345. Editor(s): Kaumaya, Pravin T. P.; Hodges, Robert S. Mayflower Scientific: Kingswinford, UK.
CODEN: 63NTAF
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Cyclic somatostatin octapeptide analogs with replacement of Lys in position 5 by Orn exhibited good retention of neuromedin B receptor affinity but >50-fold loss of SRIF receptor affinity on transfected cells and SSTR2 receptors on pancreatic AR42J cells. Further side-chain shortening by another CH2 using .alpha.,.gamma.-diaminobutyric acid substitution was even more successful in dissocg. affinities since SRIF receptor affinity decreased by >1000-fold. Necessity for a basic group in the side-chain was apparent from the loss of affinity with an ALA substitutes analog but retention of binding with an Arg substitution. All active peptides were able to block NMB-stimulated inositol phosphate prodn. with IC50 values in good agreement with binding data and all had

little affinity for the bombesin/GRP receptor.

IT 120796-15-8

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**somatostatin**-based neuromedin B receptor antagonists with
dissozn. of neuromedin B and **somatostatin** receptor binding)

L8 ANSWER 36 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:665145 HCAPLUS

DOCUMENT NUMBER: 125:318047

TITLE: A tumor-selective somatostatin analog (TT-232) with
strong in vitro and in vivo antitumor activity

AUTHOR(S): Kerl, Gy; Erchegyi, J.; Horvath, A.; Mezo, I.; Idei,
M.; Vantus, T.; Balogh, A.; Vadasz, Zs.; Boekoenyi,
Gy.; et al.

CORPORATE SOURCE: Dep. Med. Chem., Jt. Res. Org. Hungarian Acad.

SOURCE: Semmelweis Univ. Med. Sch., Budapest, 1444, Hung.

Proceedings of the National Academy of Sciences of the
United States of America (1996), 93(22), 12513-12518

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We report a series of new in vitro and in vivo data proving the selective
antitumor activity of our somatostatin structural deriv., TT-232. In
vitro, it inhibited the proliferation of 20 different human tumor cell
lines in the range of 50-95% and induced a very strong apoptosis. In vivo
TT-232 was effective on transplanted animal tumors (Colon 26, B16
melanoma, and S180 sarcoma) and on human tumor xenografts. Treatment of
MDA-MB-231 human breast cancer xenografted in mice with low submaximal
doses of TT-232 [0.25 and 0.5 mg/kg of body wt. (b.w.)] caused an av. 80%
decrease in the tumor vol. resulting in 30% tumor-free animals surviving
for longer than 200 days. Treatment of prostate tumor (PC-3) xenografted
animals with 20 mg/kg of b.w. of TT-232 for 3 wk resulted in 60% decrease
in tumor vol. and 100% survival even after 60 days, while 80% of
nontreated animals perished. We have demonstrated that TT-232 did not
bind to the membrane prepn. of rat pituitary and cortex and had no
antiseecretory activity. TT-232 was not toxic at a dose of 120 mg/kg of
b.w. in mice. Long-term incubation (24 h) of tumor cells with TT-232
caused significant inhibition of tyrosine kinases in good correlation with
the apoptosis-inducing effect. The level of p53 or KU86 did not change
following TT-232 treatment, suggesting a p53-independent apoptotic effect.
Preincubation of human breast cancer cells (MDA-MB-453) with TT-232 for 2
h decreased the growth factor receptor autophosphorylation. All of these
data suggest that TT-232 is a promising and selective antitumor agent.

IT 152510-40-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(antitumor activity of tumor-selective **somatostatin** analog
TT-232)

L8 ANSWER 37 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:89572 HCAPLUS

DOCUMENT NUMBER: 124:136089

TITLE: Intracerebroventricular injection of somatostatin sst5
receptor agonist inhibits gastric acid secretion in
rats

AUTHOR(S): Martinez, Vicente; Coy, David H.; Lloyd, K. C. Kent;
Tache, Yvette

CORPORATE SOURCE: CURE: Digestive Diseases Research Center, VA Medical
Center, Department of Medicine and Brain Research
Institute, UCLA, Los Angeles, CA, 90073, USA

SOURCE: European Journal of Pharmacology (1996), 296(2),

153-60
 CODEN: EJPHAZ; ISSN: 0014-2999
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Somatostatin and its analogs act in the brain to influence gastric acid secretion. Five different somatostatin receptor subtypes have been characterized (sst1 to sst5). We studied the influence of somatostatin (0.18-0.6 nmol/rat) and selective sst2, sst3 and sst5 receptor ligands on basal gastric acid secretion in conscious rats equipped with chronic gastric and intracerebroventricular (i.c.v.) cannulae. Somatostatin-14 (0.36 nmol/rat), the sst2, sst3 and sst5 receptor agonist, Des-AA1,2,4,5,12,13-[D-Trp8,D-Cys14]somatostatin (SMS 201-995) (0.18-0.36 nmol/rat) and the sst5 receptor agonist, BIM-23052, (0.8-1.2 nmol/rat) injected i.c.v. inhibited gastric acid secretion. Maximal inhibition reaching 42%, 60% and 42% was induced by somatostatin-14 (0.36 nmol/rat), SMS 201-995 (0.18 nmol/rat) and BIM-23052 (0.8 nmol/rat), resp. The sst2 receptor agonist, DC 32-87 (0.2-0.8 nmol/rat) and sst3 receptor agonist, BIM-23056 (0.2-1.2 nmol/rat), did not modify gastric acid secretion, except the sst3 receptor agonist at 0.4 nmol/rat which increased acid output at 20 min post-injection. The sst2 receptor agonists (0.4 nmol/rat) co-injected i.c.v. with a subthreshold dose of sst5 agonist (0.4 nmol/rat) inhibited gastric acid secretion. These results show that i.c.v. injection of somatostatin-14 inhibits basal gastric acid secretion in conscious rats through an action on sst5 receptor subtype which can be potentiated by sst2 receptor subtype.

IT 173484-74-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (somatostatin receptor subtypes involved in inhibition of gastric acid secretion)

L8 ANSWER 38 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:966879 HCAPLUS

DOCUMENT NUMBER: 124:75755

TITLE: Morphine cross-reacts with somatostatin receptor SSTR2 in the T47D human breast cancer cell line and decreases cell growth

AUTHOR(S): Hatzoglou, Anastassia; Ouafik, L'Houcine; Bakogeorgou, Efsthathia; Thermos, Kyriaki; Castanas, Elias
 CORPORATE SOURCE: School Medicine, University Crete, Crete, GR-71110, Greece

SOURCE: Cancer Research (1995), 55(23), 5632-6

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In a previous study, we found that morphine decreases, in a dose-dependent manner, the cell growth of T47D human breast cancer cells, despite the lack of .mu. opioid receptors and an interaction of morphine with other opioid sites. We have therefore examd. a possible interaction of morphine with other membrane receptor systems of the cell. The present study describes for the first time an interaction between .mu.-acting opioid drugs and the somatostatinergetic system. We have found that [125I]Tyr11-somatostatin binds with high affinity to T47D cells. Anal. of the binding data showed the presence of two components: one with high affinity but low capacity (Kd, 0.145 nM; 1450 sites/cell), and another of lower affinity but higher capacity (Kd, 1.192 nM; 11,920 sites/cell). Somatostatin-14 and somatostatin-28 showed multiphasic displacement curves, indicating heterogeneity of binding sites. The latter was confirmed by reverse transcription-PCR, with revealed the existence of the somatostatin receptor subtypes 2 and 3 (SSTR2 and SSTR3), with a relative mRNA concn. of 85 and 15%, resp. Morphine and the morphinomimetic peptide

morphiceptine (Tyr-Pro-Phe-Pro-NH₂) displace somatostatin from its binding sites. Further anal. indicated that μ -acting opioids interact with the SSTR2 receptor subtypes.

IT 150957-55-4, BIM 23034C

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(morphine cross-reaction with **somatostatin** receptor SSTR2 in T47D human breast cancer cell line and inhibition of cell growth)

L8 ANSWER 39 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:452298 HCAPLUS

DOCUMENT NUMBER: 124:49695

TITLE: Somatostatin derivatives and their radiolabelled products

INVENTOR(S): McBride, William; Dean, Richard T.

PATENT ASSIGNEE(S): Diatech, Inc., USA

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 44

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9503330	A1	19950202	WO 1994-US8335	19940721
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5620675	A	19970415	US 1993-95760	19930721
AU 9475506	A1	19950220	AU 1994-75506	19940721
AU 684823	B2	19980108		
JP 09501419	T2	19970210	JP 1994-505359	19940721
EP 804481	A1	19971105	EP 1994-925686	19940721
EP 804481	B1	20030416		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, IE				
US 6241965	B1	20010605	US 1996-586670	19960422
PRIORITY APPLN. INFO.:				
			US 1993-95760	A 19930721
			US 1992-902935	A2 19920623
			WO 1994-US8335	W 19940721

OTHER SOURCE(S): MARPAT 124:49695

AB Linear peptide derivs. and analogs of somatostatin radiolabeled with ^{99m}Tc are useful as scintigraphic imaging agents. Linear peptide derivs. and analogs of somatostatin radiolabeled with cytotoxic radioisotopes such as ¹⁸⁶Re and ¹⁸⁸Re are useful as radiotherapeutic agents. Methods and kits for making, radiolabeling, and using such peptides diagnostically and therapeutically in a mammal are provided.

IT 153314-03-5D, complexes with radioelements 161888-99-9D, complexes with radioelements 161889-27-6D, complexes with radioelements 161889-29-8D, complexes with radioelements 161889-30-1D, complexes with radioelements

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**somatostatin** derivs. and radiolabeled products for imaging and therapy)

L8 ANSWER 40 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1994:404151 HCAPLUS

DOCUMENT NUMBER: 121:4151

TITLE: Application of peptide/cell receptor kinetics utilizing radiolabeled somatostatin congeners in the in situ, in vivo detection and differentiation of neoplastic tissue

INVENTOR(S): O'Dorisio, Thomas M.; Martin, Edward W., Jr.;
 O'Dorisio, M. Sue; Woltering, Eugene A.
 PATENT ASSIGNEE(S): Ohio State University Research Foundation, USA
 SOURCE: Eur. Pat. Appl., 37 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 588754	A1	19940323	EP 1993-630068	19930914
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07304691	A2	19951121	JP 1993-228520	19930914
IL 107005	A1	19971120	IL 1993-107005	19930914
CA 2107074	AA	19940316	CA 1993-2107074	19930915
AU 9347461	A1	19940324	AU 1993-47461	19930915
AU 668210	B2	19960426		

PRIORITY APPLN. INFO.: US 1992-945110 19920915
 US 1993-114675 19930831

AB Broadly, the present invention is directed to a method for the detection and differentiation of neoplastic tissue in a patient suspected of having neoplastic tissue. The method includes the administration of a radiolabeled somatostatin congener to the patient and accessing the patient with a radiation detection probe for detg. tissue exhibiting elevated levels of radiation, viz., neoplastic tissue. However, before subjecting the patient to such administration, an initial detn. preferably is made as to whether the radiolabeled somatostatin congener will bind to the tumor site, i.e., whether somatostatin receptors are assocd. with the neoplastic tissue. This is conveniently done with a wide variety of endocrine tumors, which release peptides or hormones, referred to as "biochem. markers.". In order to make this detn., initially a biochem. marker-inhibiting dose of unlabeled somatostatin congener is administered to the patient. The biochem. marker assocd. with the neoplastic tissue then is monitored to det. whether the administered somatostatin congener reduces the presence of the marker in the patient. If the monitored presence of the marker was reduced, then the surgeon can be confident that the neoplastic tissue or tumor contains receptors to which the somatostatin will bind. Thus, the administration of radiolabeled somatostatin congener is appropriate for such patient. If the biochem. marker assocd. with the neoplastic tissue is not appropriately reduced following the administration of the unlabeled somatostatin congener, then the neoplastic tissue may not be determinable by the use of radiolabeled somatostatin congener and alternative modalities of treatment should be considered, such as the use of radiolabeled antibodies as proposed in U.S. Patent No. 4,782,840. If the tumor is of a type that does not release a biochem. marker, the presence of somatostatin receptors can be confirmed by other means, such as pathol., immunohistochem., radioreceptor assay, or such other means as will be apparent to those skilled in the art. When a patient was challenged with unlabeled octreotide acetate, the level of gastrin-releasing peptide dropped from 10,500 to 297 pg/mL, indicating somatostatin receptors assocd. with the tumor. The patient was administered 125I-Tyr3-octreotide and scanned with a Neoprobe RIGS model 1000 portable radiation detector at the time of surgery to detect a primary small bowel tumor and its metastatic deposits. The probe facilitated tumor detection and led to more effective cytoredn.

IT 132609-33-7, Lantreotide

RL: BIOL (Biological study)

(as **somatostatin** congener, in radioassay to detect cancer and metastases, surgery in relation to)

ACCESSION NUMBER: 1994:290830 HCAPLUS
DOCUMENT NUMBER: 120:290830
TITLE: Neuromedin B receptor antagonists
INVENTOR(S): Coy, David H.; Taylor, John E.
PATENT ASSIGNEE(S): Administrators of the Tulane Educational Fund, USA;
Biomeasure, Inc.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9402163	A1	19940203	WO 1993-US7036	19930727
W: AU, CA, CZ, FI, HU, JP, NO, PL, PT, RU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5462926	A	19951031	US 1993-78419	19930617
EP 606463	A1	19940720	EP 1993-918408	19930727
EP 606463	B1	20011004		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 06511495	T2	19941222	JP 1993-504762	19930727
AU 672426	B2	19961003	AU 1993-47871	19930727
AU 9347871	A1	19940214		
AT 206307	E	20011015	AT 1993-918408	19930727
NO 9401123	A	19940325	NO 1994-1123	19940325
PRIORITY APPLN. INFO.:				
			US 1992-919537	A 19920727
			US 1993-78419	A 19930617
			WO 1993-US7036	W 19930727

OTHER SOURCE(S): MARPAT 120:290830

AB A method of selectively inhibiting biochem. activity of cells induced by neuromedin B comprises contacting cells which contain neuromedin B receptors with a cyclic octapeptide, D-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Nal-NH₂ (I), or an analog thereof. Certain somatostatin octapeptide analogs function as neuromedin B receptor antagonists and have >100-fold higher affinity for neuromedin B receptors than for gastrin-releasing peptide receptors. The most potent analog, I, inhibited binding of radioliodinated [D-Tyr⁰]neuromedin B to receptors on neuromedin B receptor-transfected 3T3 cells (K_d 216 nM) and on glioblastoma C-6 cells (D_d 59 nM). Structure-function studies with I analogs indicated that the stereochem. at positions 1, 2, 7, and 8; the hydrophobicity and ring size of the substitution at positions 1, 3, and 4; and the basicity of the group at position 5 all were important in detg. receptor affinity.

IT 154827-61-9 154896-98-7 154896-99-8
154897-00-4 154897-01-5 154897-02-6
154897-03-7 154897-04-8 154897-05-9
154897-07-1 154897-09-3 154897-10-6
154897-11-7 154897-12-8 154897-13-9
154897-14-0 154942-39-9

RL: BIOL (Biological study)
(somatostatin octapeptide analog, neuromedin B receptor antagonist activity of)

IT 154896-98-7
RL: BIOL (Biological study)
(somatostatin octapeptide, neuromedin B receptor antagonist activity of)

L8 ANSWER 42 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:73774 HCAPLUS
DOCUMENT NUMBER: 118:73774
TITLE: Analogs of somatostatin bind selectively to brain somatostatin receptor subtypes

AUTHOR(S): Raynor, Karen; Coy, David C.; Reisine, Terry
 CORPORATE SOURCE: Sch. Med., Univ. Pennsylvania, Philadelphia, PA,
 19104, USA
 SOURCE: Journal of Neurochemistry (1992), 59(4), 1241-50
 CODEN: JONRA9; ISSN: 0022-3042
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The present study examd. the selectivities of a series of structurally diverse somatostatin (SRIF) analogs for SRIF receptor subtypes. SRIF receptors were labeled by 125I-Tyr11-SRIF, which has indistinguishable affinities for SRIF receptor subtypes. The inhibition by MK-678 was incomplete, indicating this peptide is highly selective for a subtype of SRIF receptor termed the SRIF1 receptor. The binding of 125I-MK-678 to SRIF1 receptors was monophasically inhibited by SRIF, the octapeptides (such as SMS-201-995), and the hexapeptides (such as MK-678), consistent with the highly selective labeling of a subtype of SRIF receptor. In contrast, the smaller CGP-23996-like analogs did not inhibit 125IMK-678 binding to SRIF1 receptors. The binding of 125I-CGP-23996 to SRIF receptors was inhibited by SRIF and the octapeptides with Hill coeffs. of <1, indicating that 125I-CGP-23996 labels multiple SRIF receptor subtypes. The hexapeptides and CGP-23996-like compds. produced only partial inhibitions of 125I-CGP-23996 binding, which were additive, indicating selective interactions of these compds. with the different receptor subpopulations labeled by 125I-CGP-23996. 125I-Tyr11-SRIF binding and 125I-CGP-23996 binding to SRIF receptors were like-wise only partially affected by 100 .mu.M GTP.gamma.S, a concn. that completely abolishes specific 125I-MK-678 binding to SRIF1 receptors. The component of 125I-CGP-23996 labeling that was sensitive to GTP.gamma.S was also MK-678 sensitive. Thus, 2 subpopulations of SRIF receptors exist in the CNS. The SRIF1 receptor is sensitive to cyclic hexapeptides such as MK-678 and to GTP.gamma.S but insensitive to smaller CGP-23996-like compds. The SRIF2 receptor is sensitive to the CGP-23996-like compds. and can be selectively labeled by 125I-CGP-23996 in the presence of high concns. of the hexapeptides or GTP.gamma.S because, unlike the SRIF1 receptor, the SRIF2 receptor is insensitive to these agents.

IT 113294-82-9 145758-77-6

RL: BIOL (Biological study)
 (somatostatin receptor subtypes of brain binding of ligands inhibition by)

L8 ANSWER 43 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1992:152405 HCAPLUS
 DOCUMENT NUMBER: 116:152405
 TITLE: Preparation of somatostatin analogs
 INVENTOR(S): Schally, Andrew V.; Janáky, Tamas; Cai, Ren Zhi
 PATENT ASSIGNEE(S): Tulane Educational Fund, Inc., USA
 SOURCE: Eur. Pat. Appl., 28 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 450480	A2	19911009	EP 1991-104845	19910327
EP 450480	A3	19911218		
EP 450480	B1	19950621		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ES 2075244	T3	19951001	ES 1991-104845	19910327
CA 2039880	AA	19911007	CA 1991-2039880	19910405
AU 9174105	A1	19911010	AU 1991-74105	19910405
AU 638118	B2	19930617		

HU 59165 A2 19920428 HU 1991-1117 19910405
 JP 06041194 A2 19940215 JP 1991-72935 19910405
 PRIORITY APPLN. INFO.: US 1990-505501 19900406

OTHER SOURCE(S): MARPAT 116:152405

GI For diagram(s), see printed CA Issue.

AB The title compds. I [Q = H, L- or D-Mel, Mel-Mel, cyclopropanealkanoic acid residue, etc.; Mel = 4-[bis(2-chloroethyl)amino]phenylalanine residue; R1 = L- or D-Phe, D-Trp, L- or D-Mel; R3 = Mel, Tyr, Phe; R6 = Thr, Val; R8 = Thr, Trp, Mel] and II [R1 = L- or D-Phe, L- or D-Trp; R3 = Phe, Trp; R6 same as defined above; R8 = Thr, Trp; A = -HNCH2(CH2)mCH(NH)(CH2)nCO-; m, n = 0, 1; Q1 = cytotoxic moiety] and their pharmaceutical acceptable salts were prepd. Successive coupling of BOC-Thr(Bzl)-OH, BOC-Cys(MBzl)-OH, BOC-Val-OH, BOC-Lys[Z(2-Cl)]-OH, BOC-D-Trp-OH, BOC-Tyr[Z(2-Br)]-OH, BOC-Cys(MBzl)-OH, and BOC-Mel-OH [Bzl = benzyl, MBzl = methylbenzyl] to a benzhydrylamine resin, cleavage of the resulting peptide from the resin, oxidn., and deprotection gave I [Q = H, R1 = Mel, R3 = R8 = Tyr, R6 = Val] (III). In an in vitro study using dispersed rat pituitary cell superfusion system the affinity consts. of III to rat cortex and prostate tumor cell membranes were 13.355 and 1.378 .times. 109M-1, resp., compared with 15.795 and 1.378 .times. 109M-1 for somatostatin (1-14).

IT **139668-80-7DP**, benzhydrylamine resin-bound **139668-81-8DP**, benzhydrylamine resin-bound **139668-82-9DP**, benzhydrylamine resin-bound **139668-83-0DP**, benzhydrylamine resin-bound **139668-84-1DP**, benzhydrylamine resin-bound **139668-84-1P**, **139668-85-2DP**, benzhydrylamine resin-bound
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as intermediate for **somatostatin** analogs)

L8 ANSWER 44 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1990:70000 HCAPLUS

DOCUMENT NUMBER: 112:70000

TITLE: Treatment of cancer with somatostatin and analogs thereof

INVENTOR(S): Taylor, John E.; Bogden, Arthur E.; Moreau, Jacques Pierre; Coy, David H.

PATENT ASSIGNEE(S): Tulane Educational Fund, Inc., USA

SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8904666	A1	19890601	WO 1988-US4126	19881118
W: JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 5073541	A	19911217	US 1988-231136	19880811
EP 344297	A1	19891206	EP 1989-901170	19881118
EP 344297	B1	19940511		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02502022	T2	19900705	JP 1988-501090	19881118
AT 105482	E	19940515	AT 1989-901170	19881118
CA 1330037	A1	19940607	CA 1988-583470	19881118
EP 414475	A1	19910227	EP 1990-309120	19900821
EP 414475	B1	19971210		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 161041	E	19971215	AT 1990-309120	19900821
ES 2110411	T3	19980216	ES 1990-309120	19900821
CA 2064705	AA	19910226	CA 1990-2064705	19900822
WO 9102820	A1	19910307	WO 1990-US4766	19900822

W: AU, CA, JP

AU 9063449	A1	19910403	AU 1990-63449	19900822
AU 655156	B2	19941208		
JP 05502156	T2	19930422	JP 1990-512531	19900822
WO 9115771	A1	19911017	WO 1991-US2225	19910329

W: AU, BB, BG, BR, CA, FI, GB, HU, JP, KP, KR, LK, MC, MG, MW, NO, PL, RO, SD, SU

RW: BF, BJ, CF, CG, CM, GA, ML, MR, SN, TD, TG

AU 9176510	A1	19911030	AU 1991-76510	19910329
AU 639560	B2	19930729		
GB 2257784	A1	19930120	GB 1992-20480	19910329
BR 9106309	A	19930420	BR 1991-6309	19910329
HU 62706	A2	19930528	HU 1992-3146	19910329
JP 05508219	T2	19931118	JP 1991-507636	19910329
JP 2733138	B2	19980330		
PL 172133	B1	19970829	PL 1991-296329	19910329
EP 450931	A1	19911009	EP 1991-302910	19910403
EP 450931	B1	19960612		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE

EP 693687	A1	19960124	EP 1995-114016	19910403
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE

AT 139343	E	19960615	AT 1991-302910	19910403
ES 2088465	T3	19960816	ES 1991-302910	19910403
NO 9203839	A	19921119	NO 1992-3839	19921001
LV 10344	B	19960220	LV 1993-4381	19930531
LT 3808	B	19960325	LT 1993-1747	19931230
US 5712087	A	19980127	US 1995-440519	19950512

PRIORITY APPLN. INFO.:

US 1987-121937	19871118
US 1988-231136	19880811
US 1985-775488	19850912
US 1986-875266	19860617
US 1987-10349	19870203
US 1987-70400	19870707
EP 1989-901170	19881118
WO 1988-US4126	19881118
US 1989-398667	19890825
US 1990-504352	19900404
WO 1990-US4766	19900822
WO 1991-US2225	19910329
EP 1991-302910	19910403
US 1992-910760	19920707

GI

D-?-naphthyl-Ala-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂



AB A method of treating a mammal suffering from cancer comprises administration of somatostatin or a somatostatin analog contg. .gtoreq.6 amino acids, in a dosage of .gtoreq.25 .mu.g/kg/day. The compds. are used to treat a solid, fast-growing tumor in a dosage of .gtoreq.250-500 .mu.g/kg/day. The somatostatin analog has a .gtoreq.4 amino acid sequence having .gtoreq.20% homol. with the core region of somatostatin and has D-Trp at position 8. The octapeptide I was prepd. in a peptide synthesizer via the intermediate t-butyloxycarbonyl-D-.beta.-naphthyl-Ala-S-methylbenzyl-Cys-Tyr-D-Trp-N.epsilon.-benzyloxycarbonyl-Lys-Val-S-methylbenzyl-Cys-O-benzyl-Thr-benzhydrylamine resin. The crude peptide in HOAc was reacted with I2 in MeOH, then purified by chromatog. on Sephadex G-25 and LRP-1 octadecylsilane. I (500 .mu.g) had a marked effect on the proliferation of human small-cell carcinoma (line NCI-H69),

a fast-growing tumor implanted in athymic mice. The agent is preferably administered directly to the site of the cancerous tumor.

IT 125184-96-5DP, resin-bound

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, in **somatostatin** analog neoplasm inhibitor prepn.)

L8 ANSWER 45 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1989:8694 HCAPLUS
DOCUMENT NUMBER: 110:8694
TITLE: Preparation of somatostatin analogs as drugs
INVENTOR(S): Bauer, Wilfried
PATENT ASSIGNEE(S): Sandoz-Patent-G.m.b.H., Fed. Rep. Ger.
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3625175	A1	19880128	DE 1986-3625175	19860725
PRIORITY APPLN. INFO.: .			DE 1986-3625175	19860725
OTHER SOURCE(S):		MARPAT 110:8694		

GI

H-D-Phe-MeCys-Phe-D-Trp-Lys-Thr-Cys-F1 II

AB ANA6CH(CH2SY1)C(:U)X1X2X3X4NHCH(CH2SY2)F [I; A = A1WA2CONA3CHZCO; A1, A3, A4 = N, (un)satd. alkyl, (substituted) Ph; A5 = H, (un)satd. alkyl; A1A5 = (CH2)4, (CH2)5; A2 = (un)satd. alkylene; A6 = H, alkyl; W = CONA4, NA5CO; Y1, Y2 = H, bond; or A = H, alkyl, phenylalkyl, RCO; R = H, alkyl, Ph, phenylalkyl; or RCO = (substituted) phenylalanyl, natural L-amino acid residue or the D-isomers thereof, dipeptide residue; A6 = H, alkyl; Y1, Y2 = H, COCRaRb(CH2)nH; n = 1-4; Ra = Me, Et; Rb = H, Me, Et, cycloalkylcarbonyl, etc; X1 = (substituted) Phe; X2 = (substituted) D- or L-Trp; X3 = Lys, .alpha.-N-methyllysyl; X4 = Thr, Ser, Val; F = hydroxymethyl carbamoyl, carboxyl, alkoxycarbonyl, prolyl, etc; U = H2, O] useful as somatostatin analogs, were prepd. Somatostatin analog II (F1 = threoninol residue), prepd. by soln.-phase peptide coupling followed by air oxidn., reduced growth hormone levels in rats by 50% at 0.12-0.21 .mu.g/kg s.c., vs. 93 .mu.g/kg s.c. for somatostatin.

IT 116430-22-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for **somatostatin** analog)

L8 ANSWER 46 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1988:611493 HCAPLUS
DOCUMENT NUMBER: 109:211493
TITLE: Preparation of somatostatin analogs as drugs
INVENTOR(S): Coy, David H.; Murphy, William A.; Heiman, Mark L.
PATENT ASSIGNEE(S): Tulane Educational Fund, Inc., USA
SOURCE: Eur. Pat. Appl., 5 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 277419	A2	19880810	EP 1987-310487	19871127
EP 277419	A3	19900214		
EP 277419	B1	19970618		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 63196599	A2	19880815	JP 1987-295911	19871124
JP 2568228	B2	19961225		
AT 154612	E	19970715	AT 1987-310487	19871127
ES 2104551	T3	19971016	ES 1987-310487	19871127
US 4853371	A	19890801	US 1988-209883	19880622
US 4904642	A	19900227	US 1989-312138	19890217
EP 414475	A1	19910227	EP 1990-309120	19900821
EP 414475	B1	19971210		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 161041	E	19971215	AT 1990-309120	19900821
ES 2110411	T3	19980216	ES 1990-309120	19900821
CA 2064705	AA	19910226	CA 1990-2064705	19900822
WO 9102820	A1	19910307	WO 1990-US4766	19900822
W: AU, CA, JP				
AU 9063449	A1	19910403	AU 1990-63449	19900822
AU 655156	B2	19941208		
JP 05502156	T2	19930422	JP 1990-512531	19900822
WO 9115771	A1	19911017	WO 1991-US2225	19910329
W: AU, BB, BG, BR, CA, FI, GB, HU, JP, KP, KR, LK, MC, MG, MW, NO, PL, RO, SD, SU				
RW: BF, BJ, CF, CG, CM, GA, ML, MR, SN, TD, TG				
AU 9176510	A1	19911030	AU 1991-76510	19910329
AU 639560	B2	19930729		
GB 2257784	A1	19930120	GB 1992-20480	19910329
BR 9106309	A	19930420	BR 1991-6309	19910329
HU 62706	A2	19930528	HU 1992-3146	19910329
JP 05508219	T2	19931118	JP 1991-507636	19910329
JP 2733138	B2	19980330		
PL 172133	B1	19970829	PL 1991-296329	19910329
EP 450931	A1	19911009	EP 1991-302910	19910403
EP 450931	B1	19960612		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP 693687	A1	19960124	EP 1995-114016	19910403
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 139343	E	19960615	AT 1991-302910	19910403
ES 2088465	T3	19960816	ES 1991-302910	19910403
NO 9203839	A	19921119	NO 1992-3839	19921001
LV 10344	B	19960220	LV 1993-4381	19930531
LT 3808	B	19960325	LT 1993-1747	19931230
US 5712087	A	19980127	US 1995-440519	19950512
PRIORITY APPLN. INFO.:			US 1987-10349	19870203
			US 1985-775488	19850912
			US 1986-875266	19860617
			US 1987-70400	19870707
			US 1988-209883	19880622
			US 1989-398667	19890825
			US 1990-504352	19900404
			WO 1990-US4766	19900822
			WO 1991-US2225	19910329
			EP 1991-302910	19910403
			US 1992-910760	19920707
OTHER SOURCE(S): MARPAT 109:211493				
AB R-A1-Cys-Tyr-D-Trp-Lys-A2-Cys-A3 (I; R = H, C1-20 alkyl; A1 = D-.beta.-Nal, D-Trp, D-X-Phe; A2 = .alpha.-aminobutyryl; A3 = Thr-NH2, Thr-OH, Nal-NH2, Trp-NH2; X = H, OH, Me, halo) and pharmaceutically acceptable salts thereof were prepd. for reducing growth hormone, insulin,				

glucagon, and/or pancreatic exocrine secretion. D-.beta.-Naphthylalanyl-
Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂ was prepd. by the solid-phase method
using BOC-protected amino acids on benzhydrylamine resin.

IT 117382-74-8P 117382-75-9P 117467-34-2P
117467-35-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as somatostatin analog)

L8 ANSWER 47 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1987:515974 HCAPLUS

DOCUMENT NUMBER: 107:115974

TITLE: Biologically active lysine-containing octapeptides

INVENTOR(S): Schally, Andrew V.; Cai, Ren Zhi

PATENT ASSIGNEE(S): Tulane Educational Fund, Inc., USA

SOURCE: Eur. Pat. Appl., 33 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 203031	A2	19861126	EP 1986-810174	19860415
EP 203031	A3	19880921		
EP 203031	B1	19920729		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4650787	A	19870317	US 1985-727105	19850425
US 4725577	A	19880216	US 1986-843539	19860328
AT 78831	E	19920815	AT 1986-810174	19860415
AU 8656338	A1	19861030	AU 1986-56338	19860417
AU 600895	B2	19900830		
DK 8601854	A	19861026	DK 1986-1854	19860422
CA 1333646	A1	19941220	CA 1986-507490	19860424
JP 61293997	A2	19861224	JP 1986-97834	19860425

PRIORITY APPLN. INFO.:

US 1985-727105 19850425
US 1986-843539 19860328
EP 1986-810174 19860415

GI

R-X-X¹-X²-Lys-X³-X⁴-R¹ I

AB The octapeptide somatostatin analogs (I; R = (acetylated) L-, D- or DL-amino acid residue selected from H-Ala, H-Val, H-Phe, p-chlorophenylalanyl, H-Trp, H-Pro, H-Ser, H-Thr, H-Tyr, H-Glu, H-.beta.-Ala, H-Abu, MeAla, 5-halotryptophanyl; R¹ = L-, D-, or DL-amino acid amide residue selected from Thr-NH₂, Val-NH₂, (hydroxy)Pro-NH₂, Ser-NH₂, 5-fluoro- or formyltryptophanamide residue, Ala-NH₂, Gly-NH₂, MeAla-NH₂; X, X⁴ = L- or D- Cys, Abu, Asp, Lys; X¹ = Phe, Tyr; X² = L-, D-, or DL-5-halotryptophan residue; X³ = Thr, Val; Abu = .alpha.-aminobutyric acid residue) and pharmaceutically acceptable salts, useful as growth hormone inhibitors, for treatment of gastrointestinal disorders, cancer therapy, and the management of diabetes, were prepd. by the solid-phase method using a benzhydrylamine resin. I in vivo were more potent inhibitors of growth hormone and insulin release than somatostatin-14 in rats.

IT 103222-03-3P 103222-04-4P 103548-90-9P
109791-07-3P 109985-47-9P 109985-51-5P

109985-54-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and cyclization of, **somatostatin** analog from)

IT **109985-49-1DP**, benzylhydriylamine resin-bound **109985-50-4DP**

, benzylhydriylamine resin-bound **109985-53-7DP**, benzylhydriylamine resin-bound **109985-56-0DP**, benzylhydriylamine resin-bound

109985-62-8DP, benzylhydriylamine resin-bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and deprotection of, **somatostatin** analog from)

L8 ANSWER 48 OF 48 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1985:160733 HCAPLUS

DOCUMENT NUMBER: 102:160733

TITLE: Inhibition of growth of a prolactin and growth hormone-secreting pituitary tumor in rats by D-tryptophan-6 analog of luteinizing hormone-releasing hormone

AUTHOR(S): Torres-Aleman, I.; Redding, T. W.; Schally, A. V.

CORPORATE SOURCE: Endocr. Lab., Veterans Adm. Med. Cent., New Orleans, LA, 70146, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1985), 82(4), 1252-6
CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of long-term administration of analogs of LH-RH and **somatostatin** on the growth of the growth hormone (GH) [9002-72-6]- and prolactin (PRL) [9002-62-4]-secreting rat pituitary GH3 tumor was investigated. Daily administration of [D-Trp6]LH-RH [57773-63-4] (50 .mu.g/day), early after inoculation of the GH3 tumor, inhibited tumor growth by >90% as compared to controls. Similarly, a single once-a-month injection of long-acting [D-Trp6]LH-RH microcapsules (in a dose calcd. to release about 25 .mu.g/day for 30 days) inhibited the growth of GH3 pituitary tumor by > 50% 6 or 13 wk after transplantation, when the tumors were fully developed. Serum GH and PRL levels also were reduced markedly by treatment with [D-Trp6]LH-RH. On the other hand, the administration of an antagonistic analog of LH-RH, N-Ac-[D-Phe(4Cl)1,2, D-Trp3, D-Arg6, D-Ala10]LH-RH, did not reduce the growth of this tumor, and the treatment with 2 different analogs of **somatostatin**, cyclo(Pro-Phe-D-Trp-Lys-Thr-Phe) [77236-35-2] and D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr NH2 [95833-38-8], appeared to enhance it. The use of [D-Trp6]LH-RH might be considered for the treatment of some pituitary tumors in patients who failed to respond to conventional therapy.

=> select hit rn 18 1-48

E1 THROUGH E191 ASSIGNED

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DICTIONARY FILE UPDATES: 8 MAY 2003 HIGHEST RN 512516-86-8

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<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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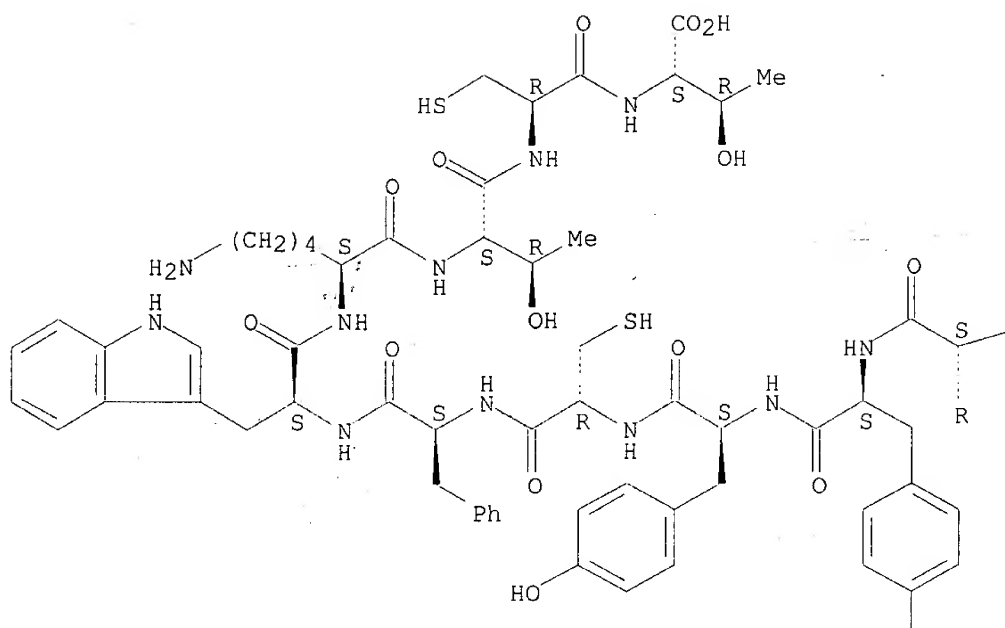
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 RN 508194-91-0 REGISTRY
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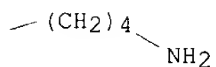
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Absolute stereochemistry.

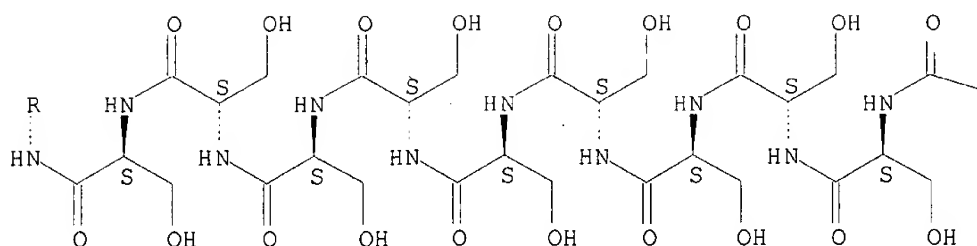
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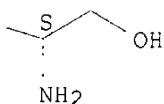
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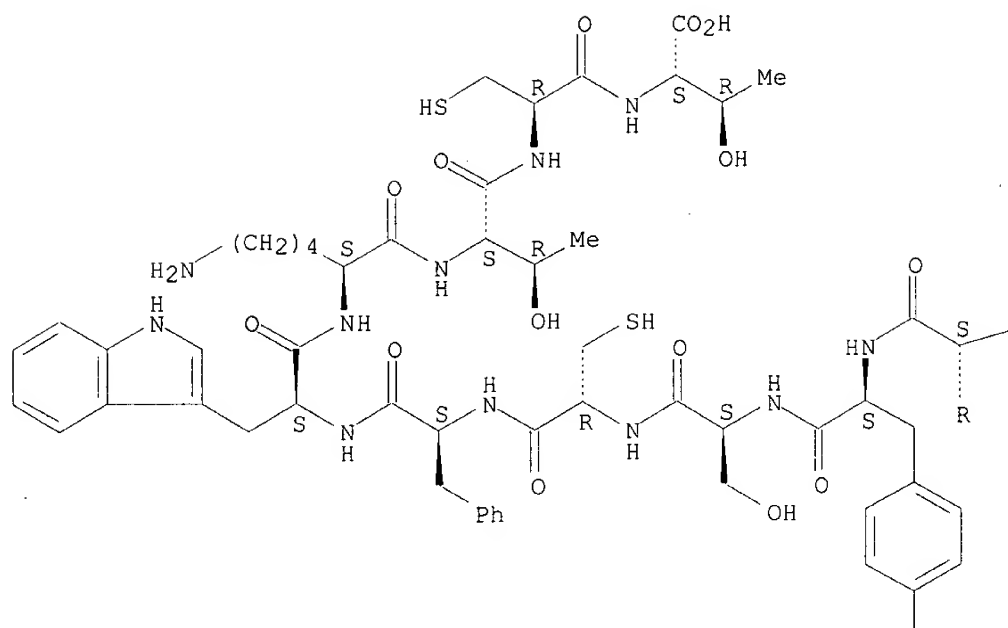
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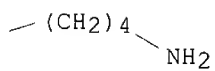
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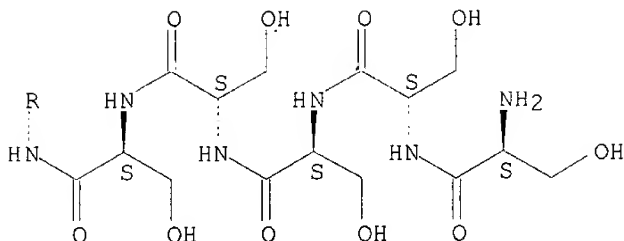
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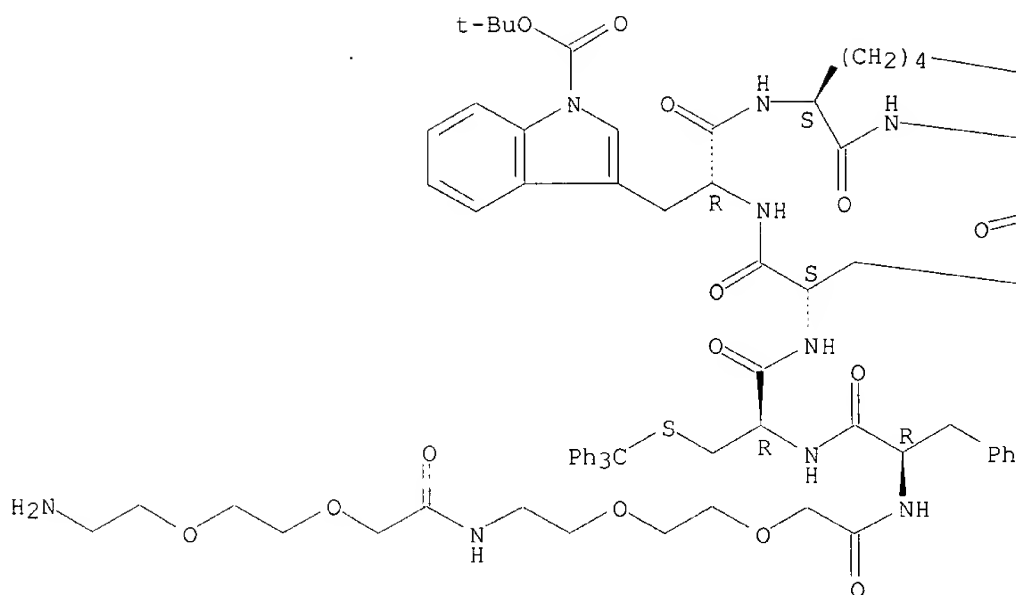
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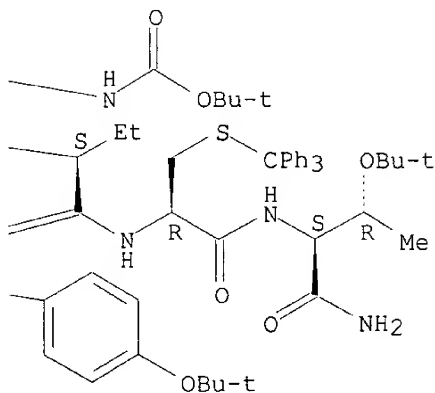
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Absolute stereochemistry.

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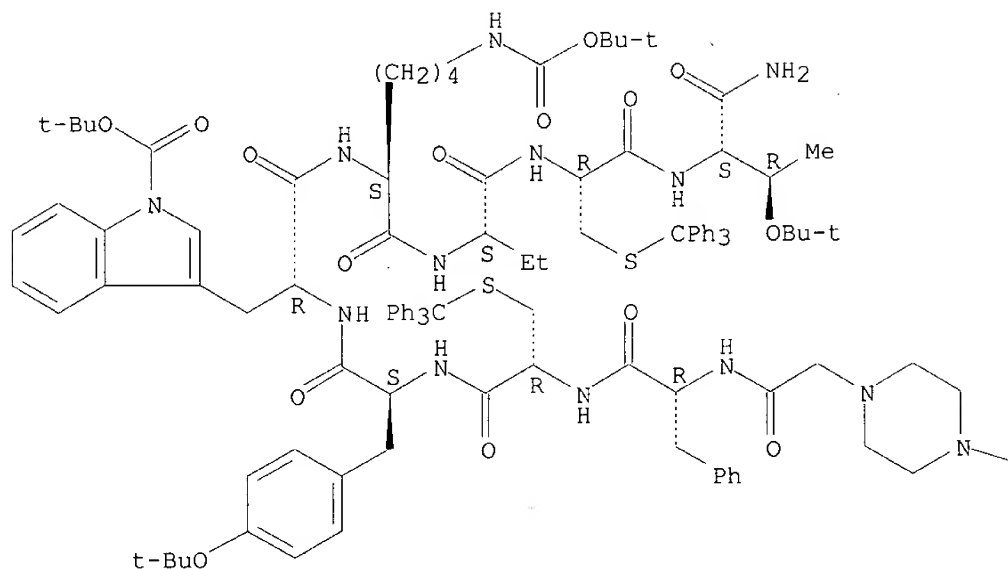
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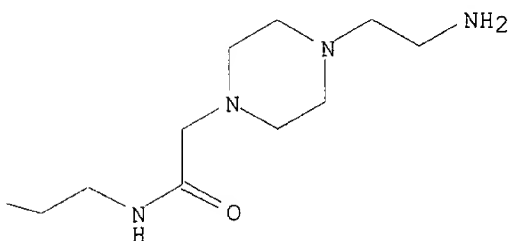
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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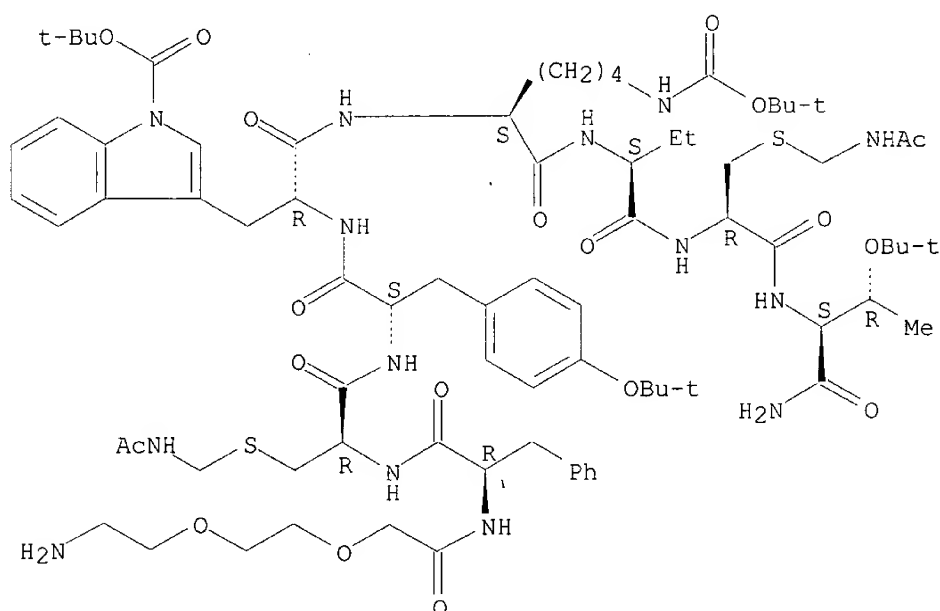
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L10 ANSWER 20 OF 191 REGISTRY COPYRIGHT 2003 ACS
 RN 478815-19-9 REGISTRY
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 dimethylethoxy)carbonyl]-D-tryptophyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-
 lysyl-(2S)-2-aminobutanoyl-S-[(acetylamino)methyl]-L-cysteinyl-O-(1,1-
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 LC STN Files: CA, CAPLUS, TOXCENTER

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

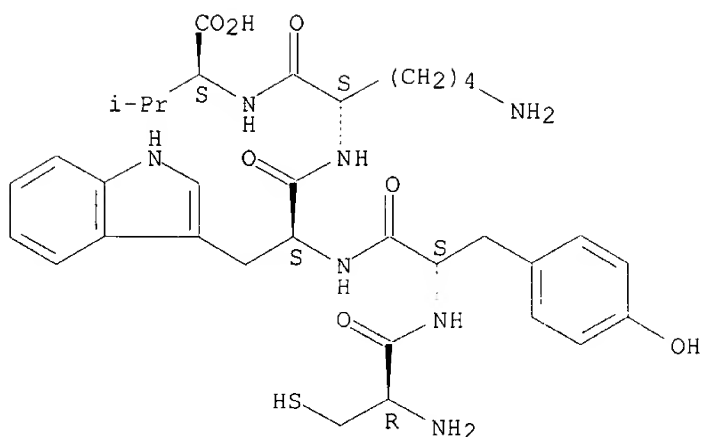


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 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:39546

L10 ANSWER 25 OF 191 REGISTRY COPYRIGHT 2003 ACS
 RN 442685-61-2 REGISTRY
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 NAME)
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 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C34 H47 N7 O7 S
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Absolute stereochemistry.



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REFERENCE 1: 137:99024

L10 ANSWER 30 OF 191 REGISTRY COPYRIGHT 2003 ACS

RN **401912-42-3** REGISTRY

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FS PROTEIN SEQUENCE; STEREOSEARCH

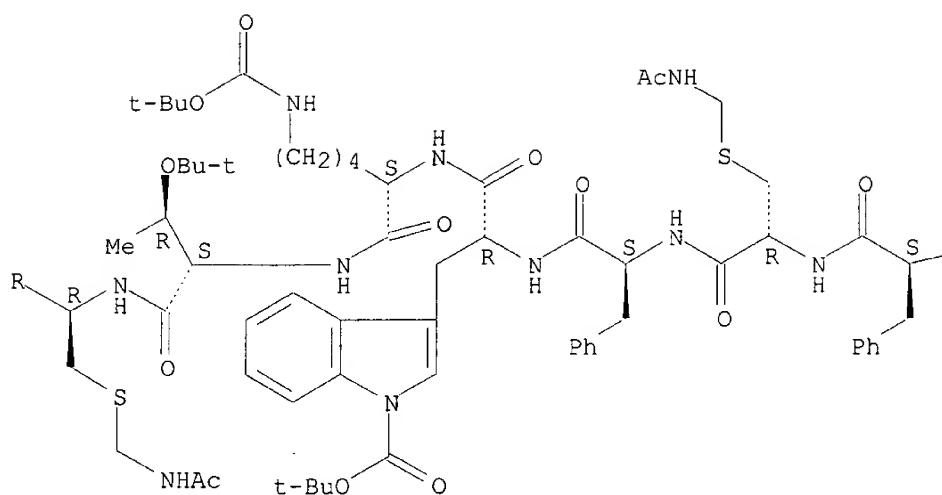
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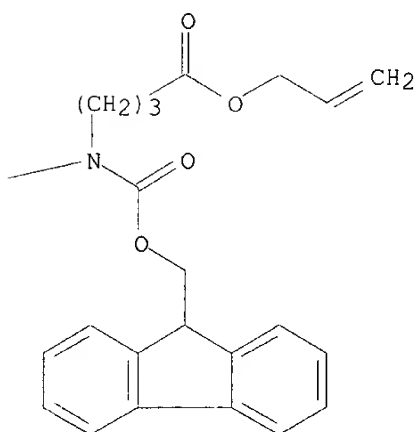
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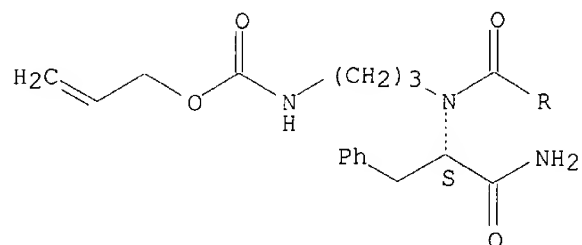
Absolute stereochemistry.



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1 REFERENCES IN FILE CA (1957 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 136:210716

L10 ANSWER 35 OF 191 REGISTRY COPYRIGHT 2003 ACS

RN 371242-05-6 REGISTRY

CN L-Threoninamide, D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-
1-aminocyclopentanecarbonyl-3-mercapto-L-valyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 6: PN: US6316414 SEQID: 6 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C53 H73 N11 O10 S2

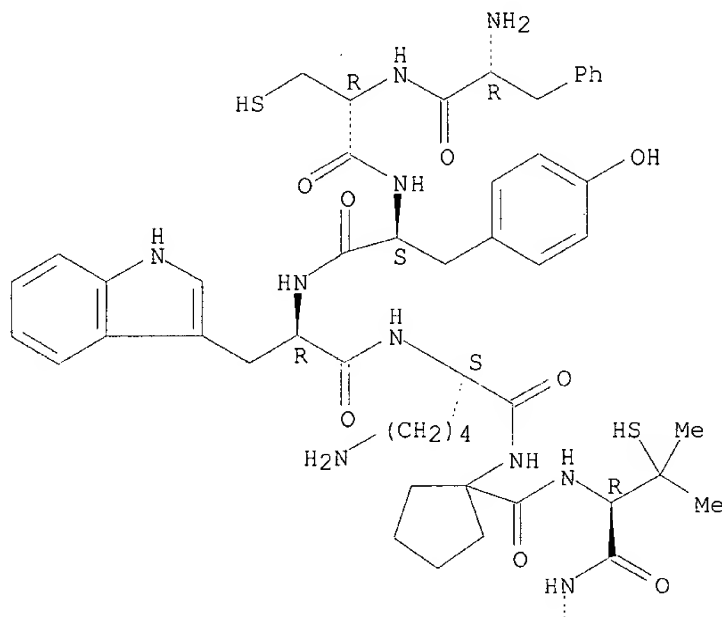
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

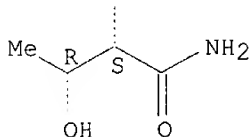
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 135:358166

L10 ANSWER 40 OF 191 REGISTRY COPYRIGHT 2003 ACS

RN 270900-25-9 REGISTRY

CN L-Isoleucine, L-glutamyl-L-histidylglycyl-L-threonyl-L-alanyl-L-prolyl-L-
.alpha.-glutamyl-L-cysteinyl-L-phenylalanyl-L-tryptophyl-L-lysyl-L-tyrosyl-
L-cysteinyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 60: PN: WO0031265 SEQID: 32 claimed protein

CN Rat urotensin II

CN Urotensin II (rat)

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C77 H107 N19 O20 S2

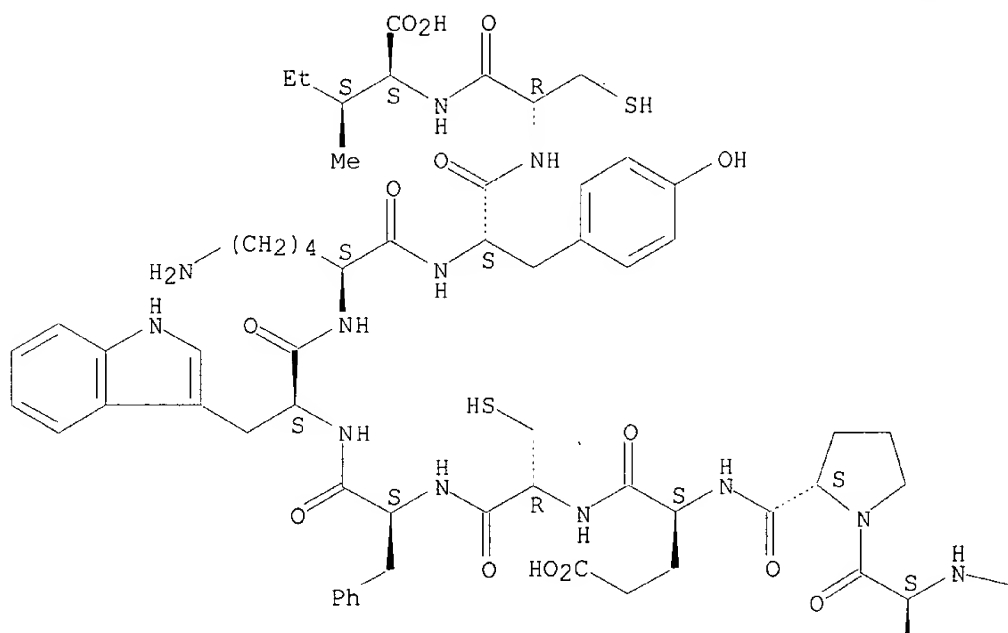
SR CA

LC STN Files: BIOSIS, CA, CAPLUS, CHEMCATS

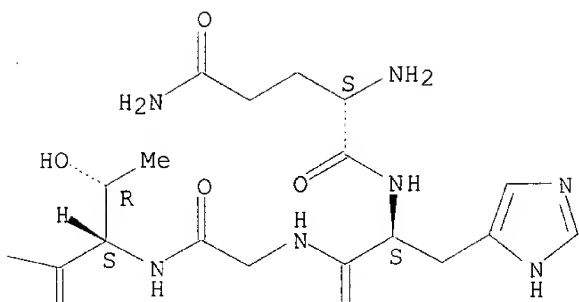
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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5 REFERENCES IN FILE CA (1957 TO DATE)
5 REFERENCES IN FILE CAPLUS (1957 TO DATE)

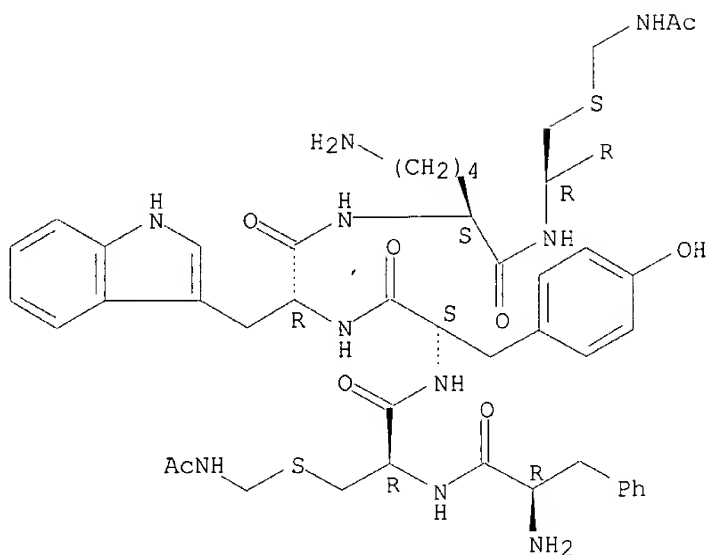
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REFERENCE 3: 137:211269
REFERENCE 4: 135:29420
REFERENCE 5: 133:13164

L10 ANSWER 45 OF 191 REGISTRY COPYRIGHT 2003 ACS
RN 250132-15-1 REGISTRY
CN Glycine, D-phenylalanyl-S-[(acetylamino)methyl]-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-S-[(acetylamino)methyl]-L-cysteinyl-L-threonyl-2-aminodecanoyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C63 H91 N13 O14 S2
SR CA

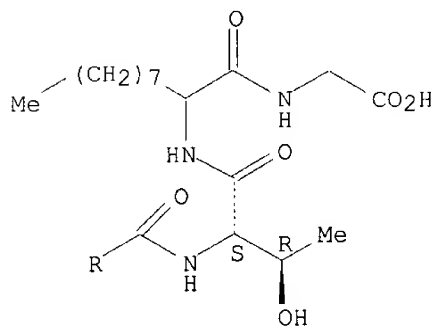
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

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1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

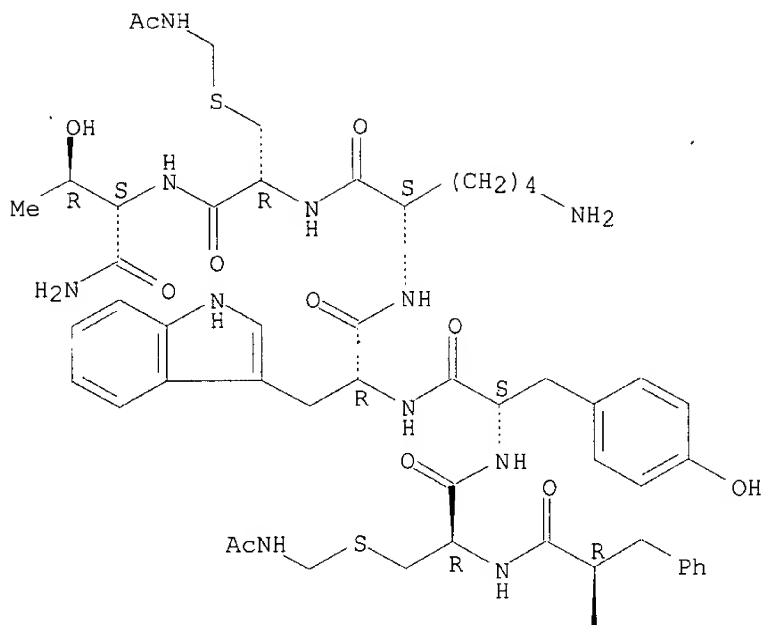
REFERENCE 1: 131:331722

L10 ANSWER 50 OF 191 REGISTRY COPYRIGHT 2003 ACS
RN 250132-09-3 REGISTRY
CN L-Threoninamide, D-phenylalanyl-S-[(acetylamino)methyl]-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-S-[(acetylamino)methyl]-L-cysteinyl- (9CI)
(CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C51 H70 N12 O11 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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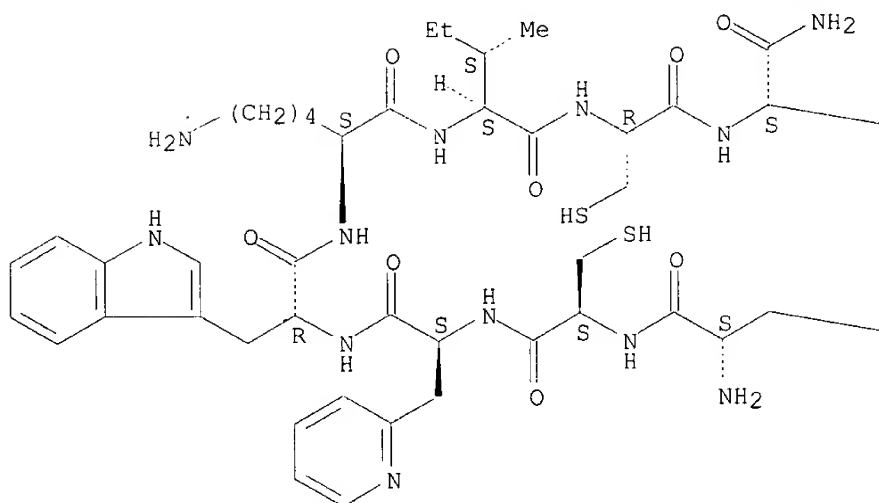
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L10 ANSWER 55 OF 191 REGISTRY COPYRIGHT 2003 ACS
RN 243470-90-8 REGISTRY
CN L-Alaninamide, 3-(2-naphthalenyl)-L-alanyl-D-cysteinyll-3-(2-pyridinyl)-L-alanyl-D-tryptophyl-L-lysyl-L-isoleucyl-L-cysteinyll-3-(2-naphthalenyl)-(9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C63 H76 N12 O8 S2
SR CA
LC STN Files: CA, CAPLUS

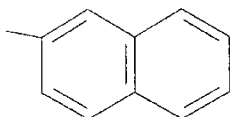
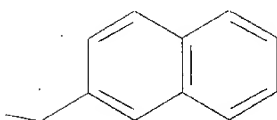
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 131:208607

L10 ANSWER 60 OF 191 REGISTRY COPYRIGHT 2003 ACS

RN **243470-85-1** REGISTRY

CN L-Alaninamide, 3-[1,1'-biphenyl]-4-yl-L-alanyl-D-cysteinyl-3-(2-pyridinyl)-
L-alanyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-3-[1,1'-biphenyl]-4-yl-
(9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C66 H78 N12 O8 S2

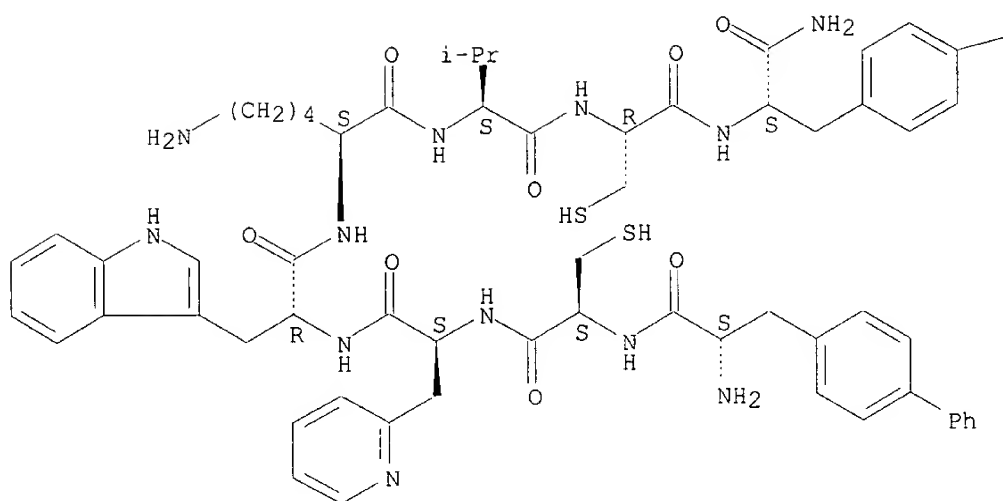
SR CA

LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 131:208607

L10 ANSWER 65 OF 191 REGISTRY COPYRIGHT 2003 ACS

RN 243470-80-6 REGISTRY

CN L-Alaninamide, 3-(2-naphthalenyl)-L-alanyl-D-cysteiny-3-(2-pyridinyl)-L-alanyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteiny-3-(2-naphthalenyl)- (9CI)
(CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C62 H74 N12 O8 S2

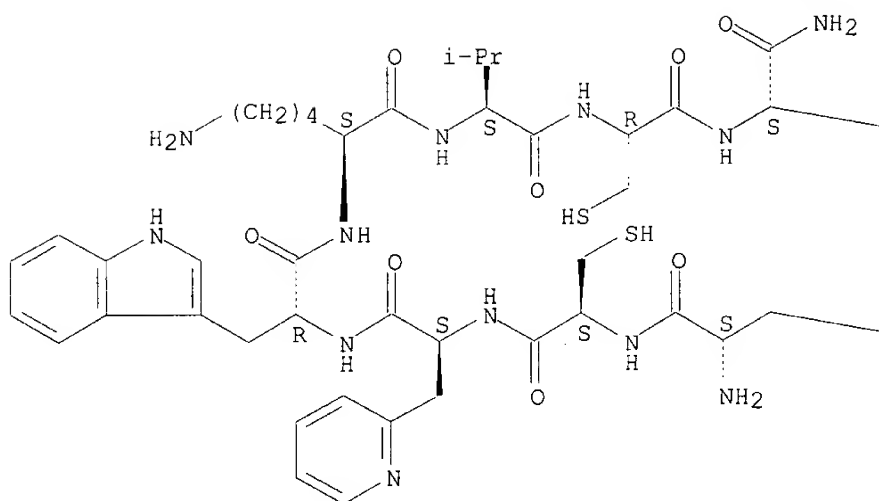
SR CA

LC STN Files: CA, CAPLUS

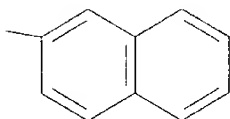
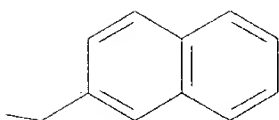
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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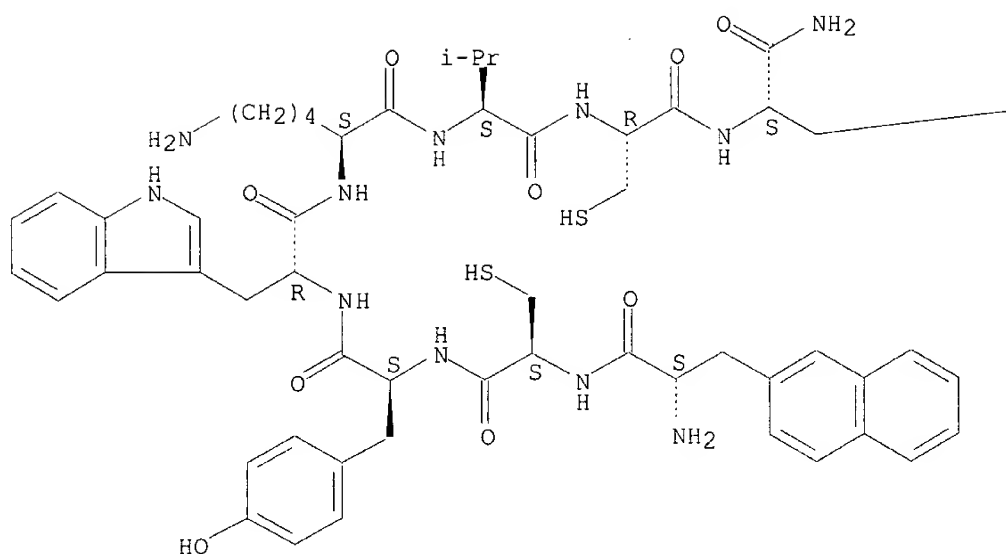
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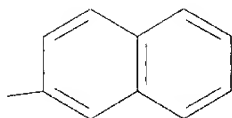
L10 ANSWER 70 OF 191 REGISTRY COPYRIGHT 2003 ACS
RN 243470-75-9 REGISTRY
CN L-Alaninamide, 3-(2-naphthalenyl)-L-alanyl-D-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C63 H75 N11 O9 S2
SR CA
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



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1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 131:208607

L10 ANSWER 75 OF 191 REGISTRY COPYRIGHT 2003 ACS

RN 223659-62-9 REGISTRY

CN L-Threoninamide, D-tyrosyl-D-tyrosyl-D-tyrosyl-D-tyrosyl-D-tyrosyl-D-tyrosyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

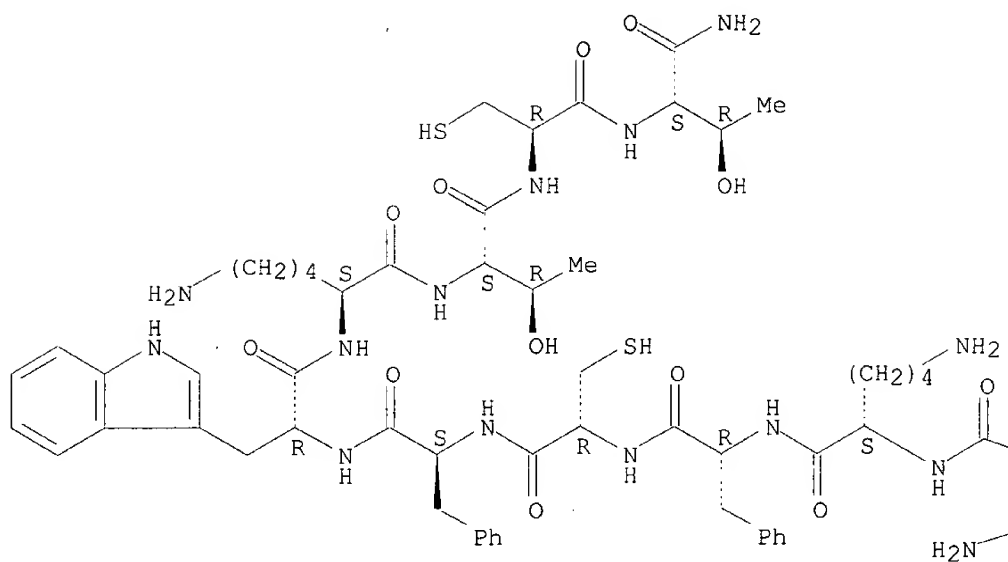
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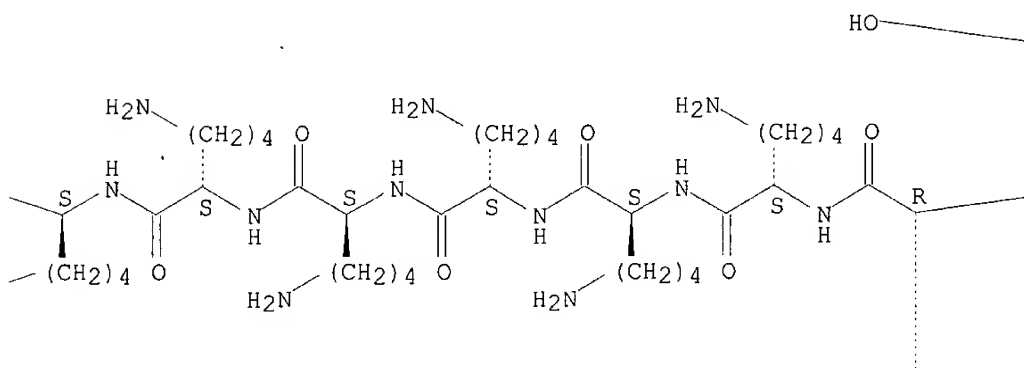
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

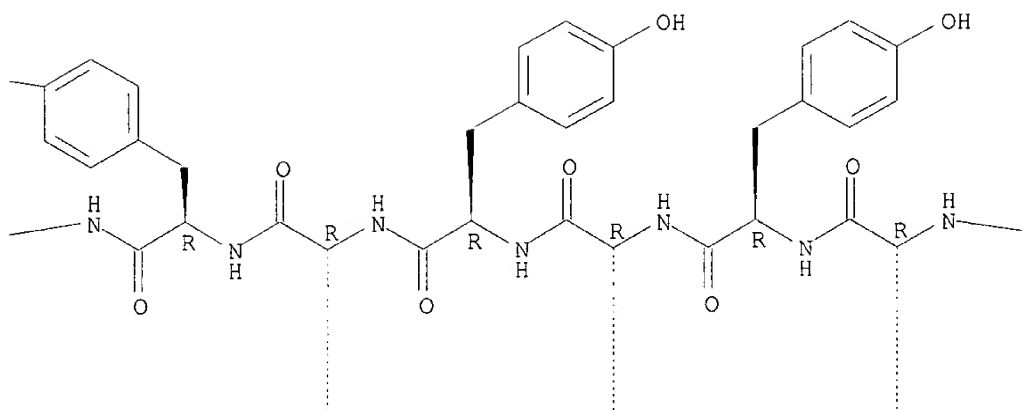
PAGE 1-A



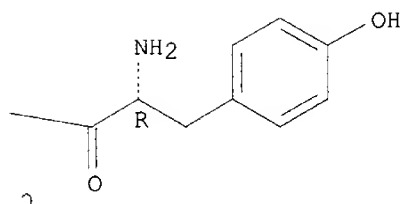
PAGE 1-B



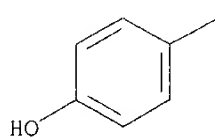
PAGE 1-C



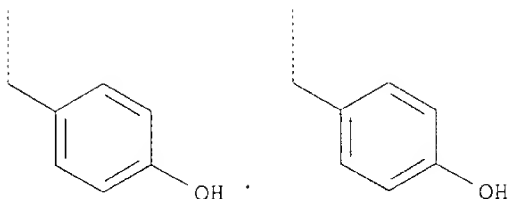
PAGE 1-D



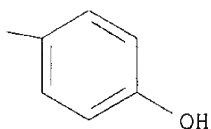
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PAGE 2-C



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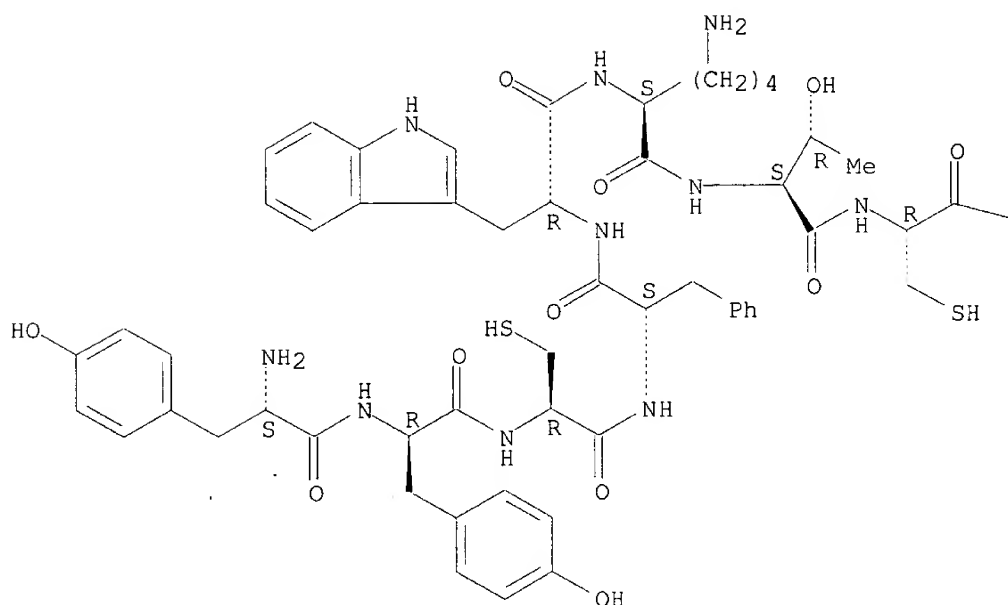
REFERENCE 1: 130:312081

L10 ANSWER 80 OF 191 REGISTRY COPYRIGHT 2003 ACS
RN 223659-57-2 REGISTRY
CN L-Threonine, L-tyrosyl-D-tyrosyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-
lysyl-L-threonyl-L-cysteinyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C58 H75 N11 O14 S2
SR CA
LC STN Files: CA, CAPLUS

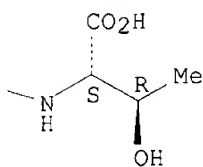
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

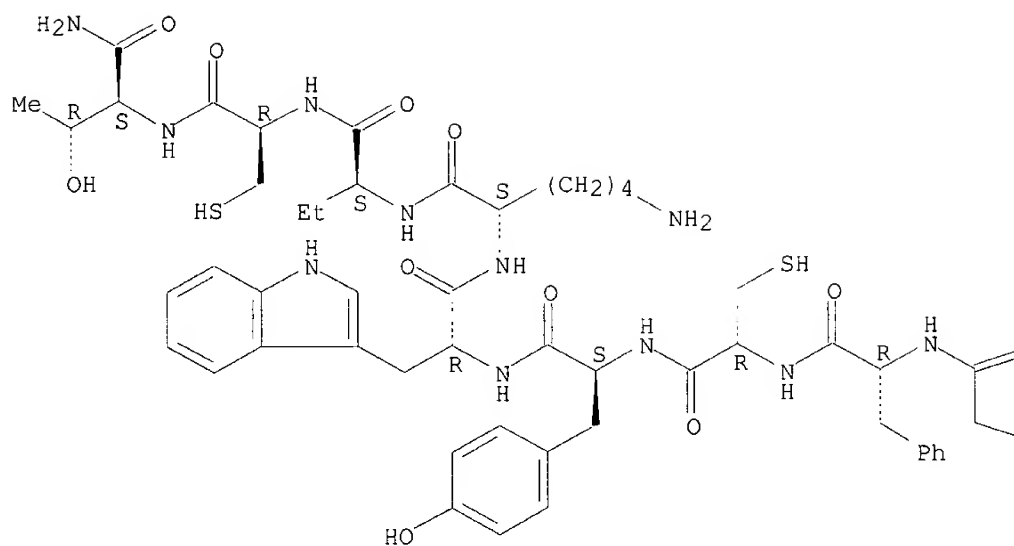
REFERENCE 1: 130:312081

L10 ANSWER 85 OF 191 REGISTRY COPYRIGHT 2003 ACS
 RN 204388-14-7 REGISTRY
 CN L-Threoninamide, N-[[4-(2-hydroxyethyl)-1-piperazinyl]acetyl]-D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-(2S)-2-aminobutanoyl-L-cysteinyl- (9CI) (CA INDEX NAME)
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C57 H81 N13 O12 S2
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

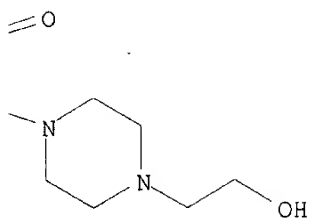
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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REFERENCE 2: 131:295567

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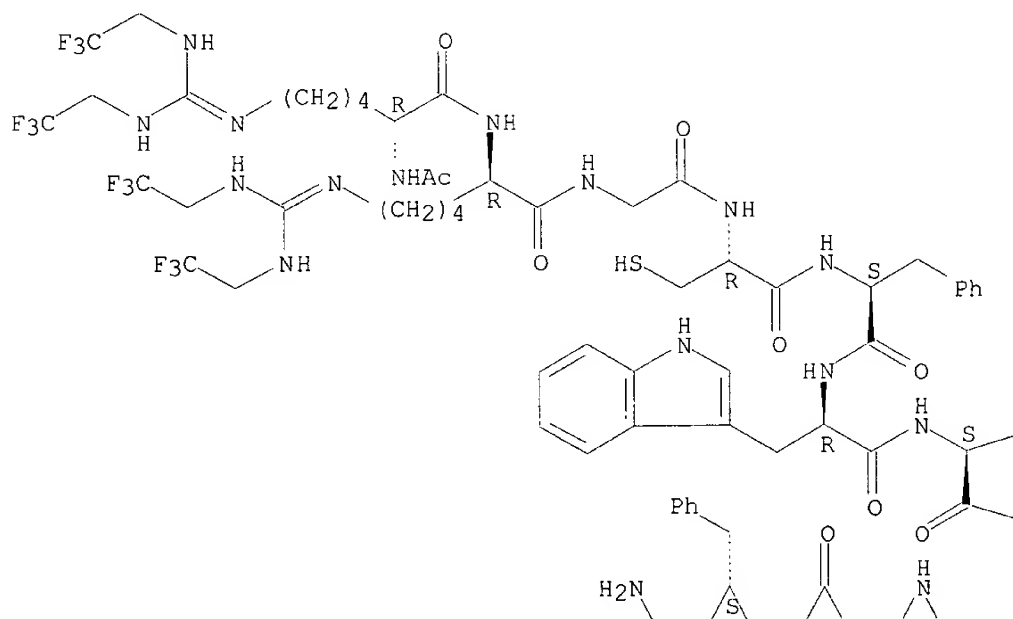
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L10 ANSWER 90 OF 191 REGISTRY COPYRIGHT 2003 ACS
 RN 204387-90-6 REGISTRY
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 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

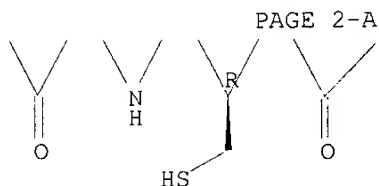
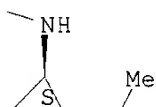
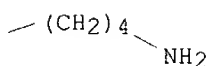
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 131:295567

REFERENCE 2: 128:226683

L10 ANSWER 95 OF 191 REGISTRY COPYRIGHT 2003 ACS

RN **204387-85-9** REGISTRY

CN L-Phenylalaninamide, N2-acetyl-N6-[bis(ethylamino)methylene]-D-lysylglycyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl-(9CI) (CA INDEX NAME)

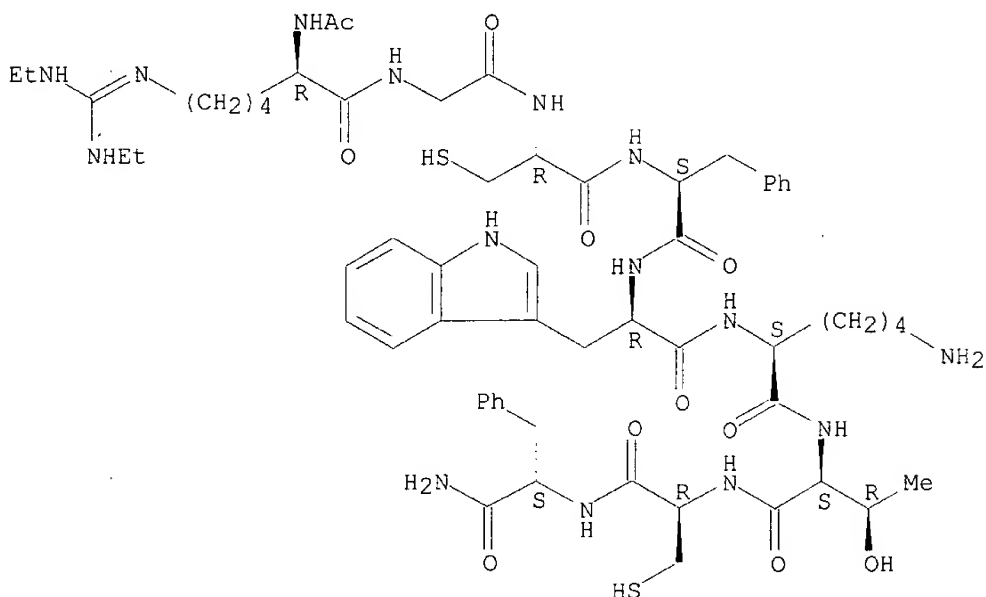
FS PROTEIN SEQUENCE; STEREOSEARCH

MF C60 H87 N15 O11 S2

SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 131:295567

REFERENCE 2: 128:226683

L10 ANSWER 100 OF 191 REGISTRY COPYRIGHT 2003 ACS

RN **204387-80-4** REGISTRY

CN L-Threoninamide, N2-acetyl-N6-[bis[(2,2,2-trifluoroethyl)amino]methylene]-D-lysylglycyl-L-cysteiny-L-phenylalanyl-D-tryptophyl-N6-methyl-L-lysyl-L-threonyl-L-cysteiny- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C56 H81 F6 N15 O12 S2

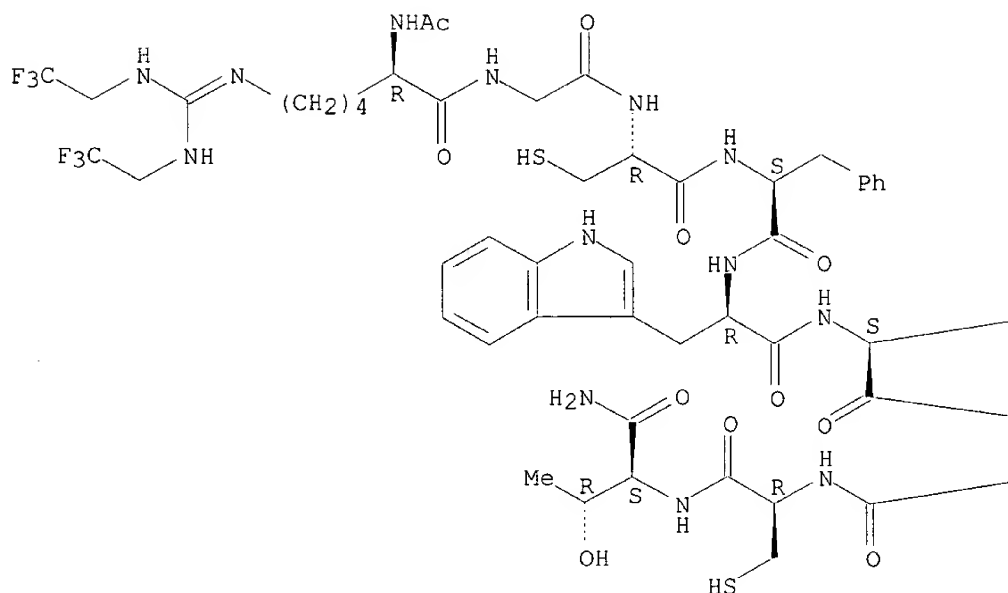
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LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

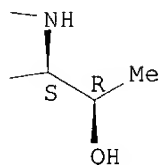
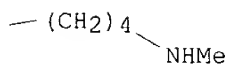
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 131:295567

REFERENCE 2: 128:226683

L10 ANSWER 105 OF 191 REGISTRY COPYRIGHT 2003 ACS

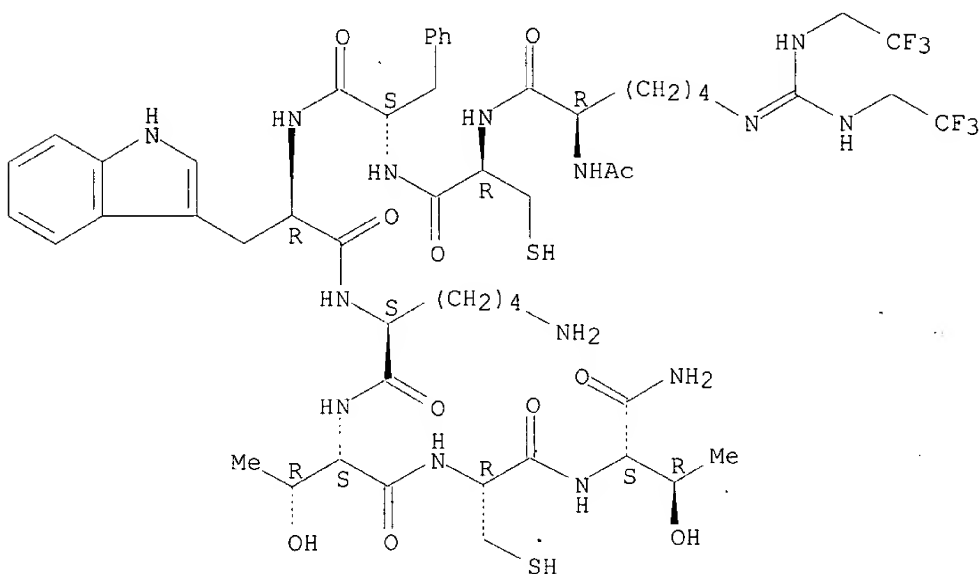
RN 204387-75-7 REGISTRY

CN L-Threoninamide, N2-acetyl-N6-[bis[(2,2,2-trifluoroethyl)amino]methylene]-

D-lysyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl- (9CI) (CA INDEX NAME)
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C53 H76 F6 N14 O11 S2
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1957 TO DATE)
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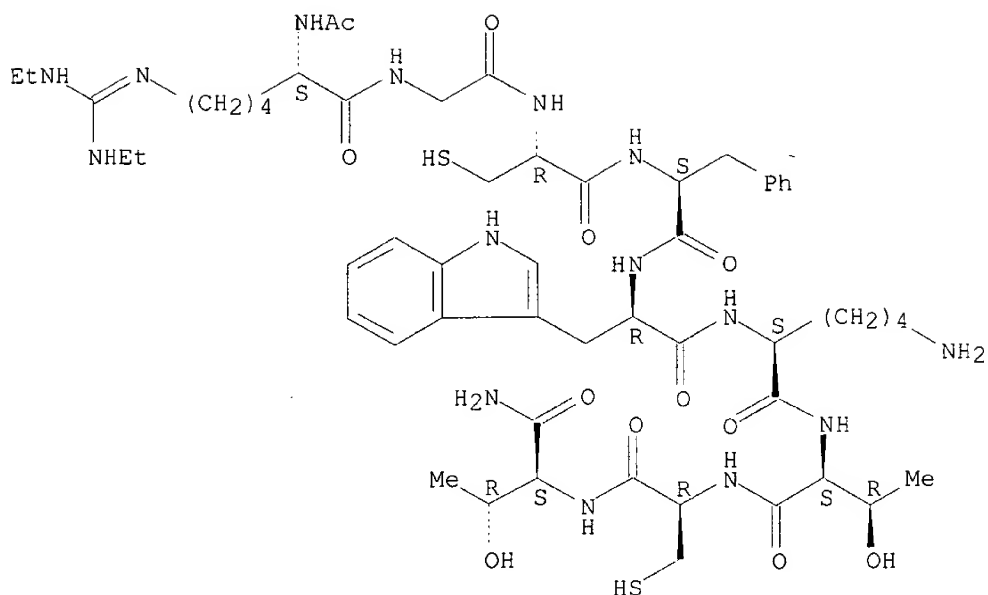
REFERENCE 1: 131:295567

REFERENCE 2: 128:226683

L10 ANSWER 110 OF 191 REGISTRY COPYRIGHT 2003 ACS
 RN 204387-70-2 REGISTRY
 CN L-Threoninamide, N2-acetyl-N6-[bis(ethylamino)methylene]-L-lysylglycyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl- (9CI) (CA INDEX NAME)
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C55 H85 N15 O12 S2
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 131:295567

REFERENCE 2: 128:226683

L10 ANSWER 115 OF 191 REGISTRY COPYRIGHT 2003 ACS

RN 204387-65-5 REGISTRY

CN L-Threonine, D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-3-mercapto-L-valyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

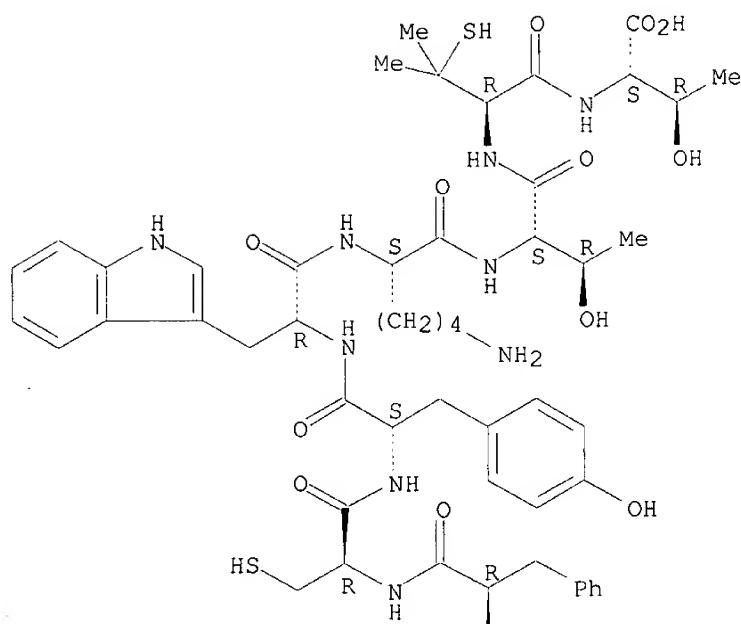
MF C51 H70 N10 O12 S2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



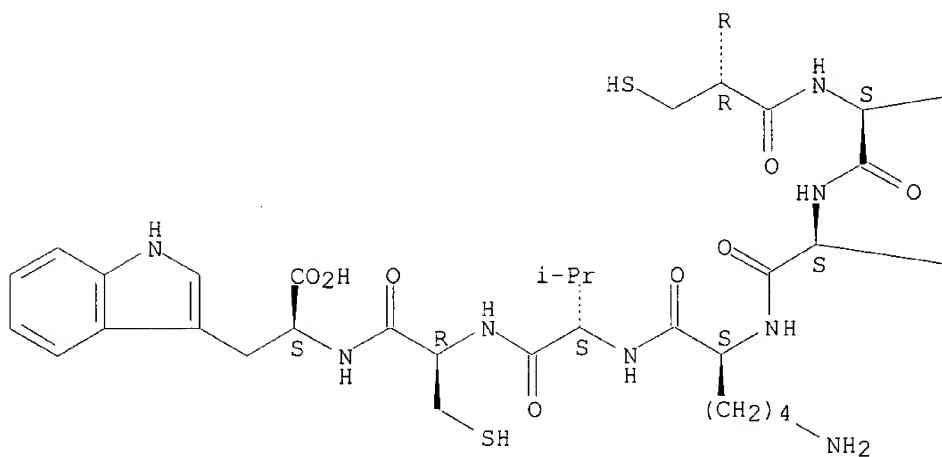
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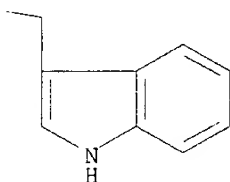
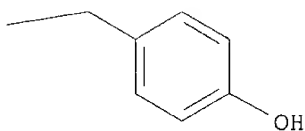
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

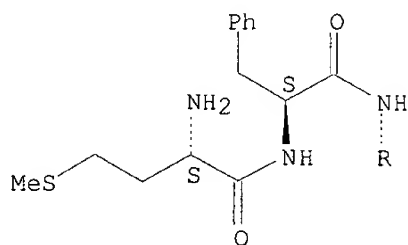
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3 REFERENCES IN FILE CA (1957 TO DATE)
3 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 133:79332

REFERENCE 2: 131:28626

REFERENCE 3: 128:162873

L10 ANSWER 125 OF 191 REGISTRY COPYRIGHT 2003 ACS

RN **186514-24-9** REGISTRY

CN L-Threoninamide, O-[(dichlorophenyl)methyl]-N-[(1,1-dimethylethoxy)carbonyl]-L-tyrosyl-L-alanyl-O-[(dichlorophenyl)methyl]-D-tyrosyl-S-[(methylphenyl)methyl]-L-cysteiny-O-[(dichlorophenyl)methyl]-L-tyrosyl-D-tryptophyl-N2-[(phenylmethoxy)carbonyl]-L-lysyl-L-valyl-S-[(methylphenyl)methyl]-L-cysteiny-N-(diphenylmethyl)-O-(phenylmethyl)-(9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE

MF C132 H141 C16 N13 O18 S2

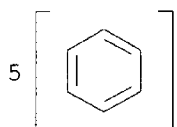
CI IDS

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

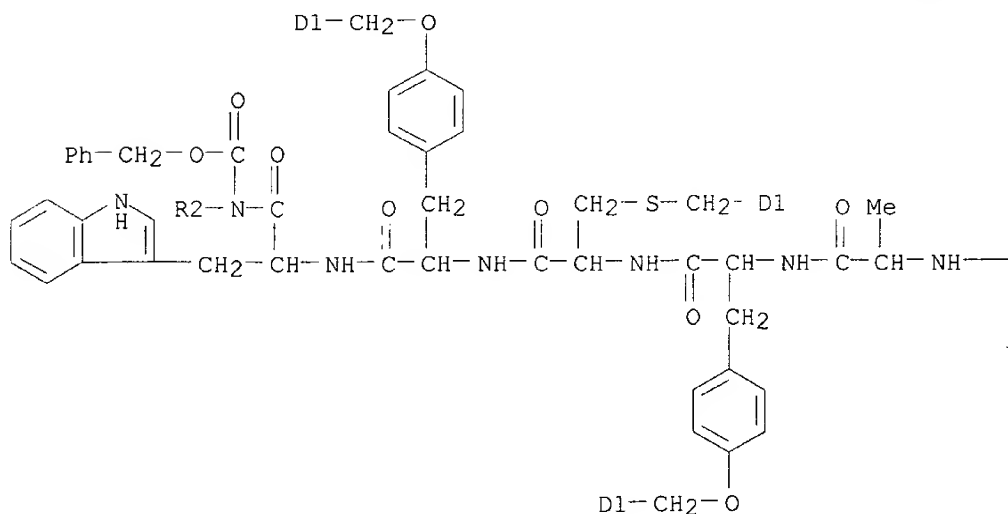
PAGE 1-A



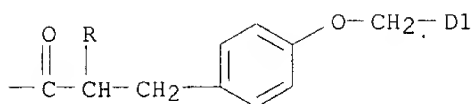
2 (D1-Me)

6 (D1-Cl)

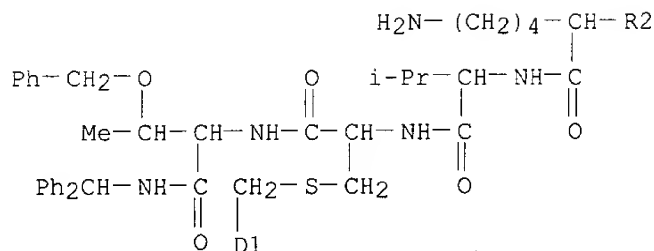
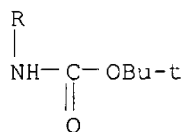
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- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

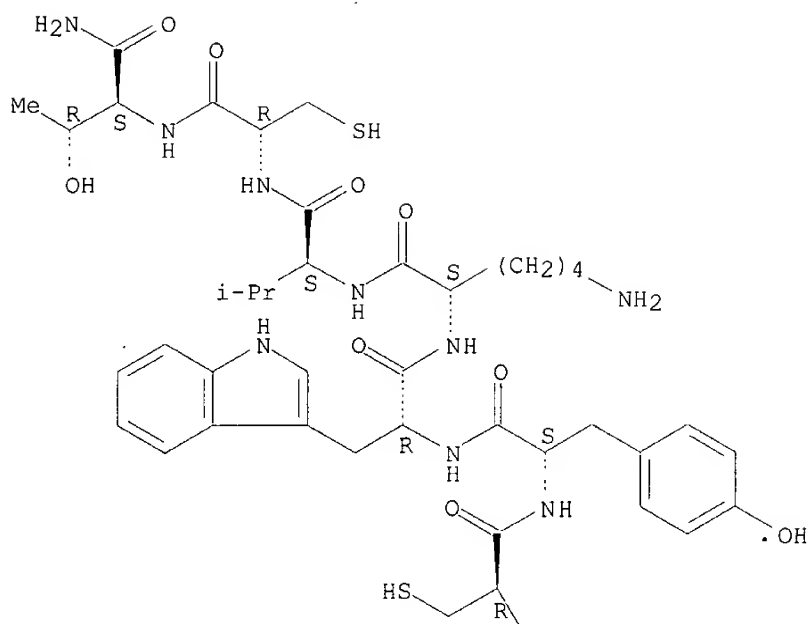
REFERENCE 1: 126:141513

L10 ANSWER 130 OF 191 REGISTRY COPYRIGHT 2003 ACS
 RN 186293-13-0 REGISTRY
 CN L-Threoninamide, L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl- (9CI) (CA INDEX NAME)
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C41 H60 N10 O9 S2
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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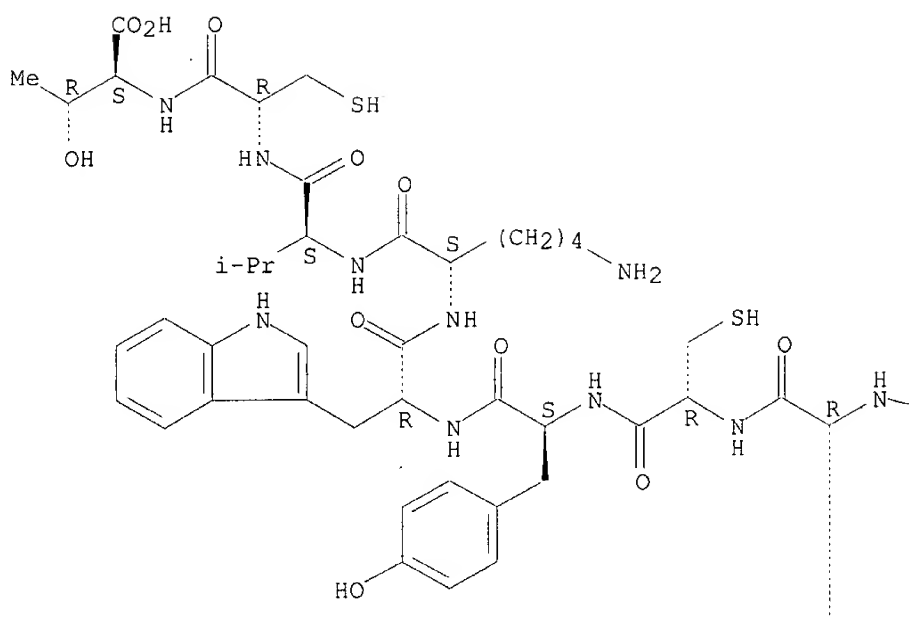


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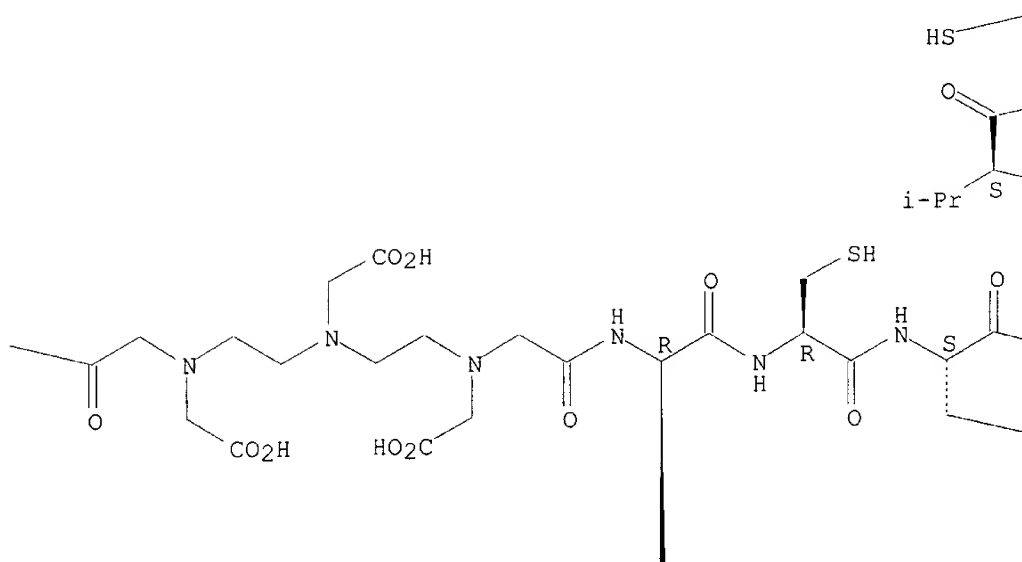
REFERENCE 1: 126:141513

L10 ANSWER 135 OF 191 REGISTRY COPYRIGHT 2003 ACS
 RN 161888-99-9 REGISTRY
 CN L-Threonine, 1,1'-[[[(carboxymethyl)imino]di-2,1-ethanediyl]bis[N-(carboxymethyl)glycyl-3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl- (9CI) (CA INDEX NAME)
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C122 H159 N23 O30 S4
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

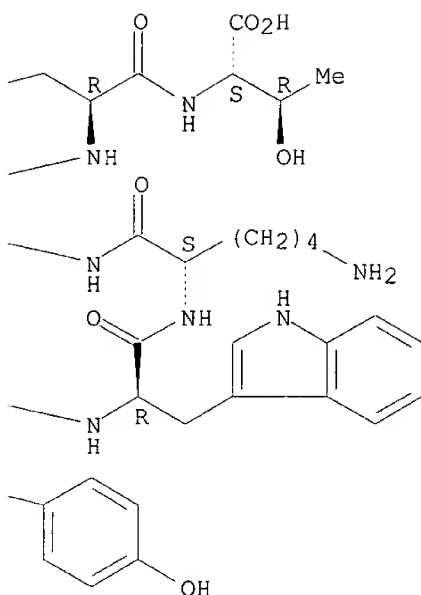
Absolute stereochemistry.



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2 REFERENCES IN FILE CA (1957 TO DATE)
 2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 126:343883

REFERENCE 2: 124:49695

L10 ANSWER 140 OF 191 REGISTRY COPYRIGHT 2003 ACS

RN **154897-11-7** REGISTRY

CN L-Alaninamide, D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-N6,N6-diethyl-L-lysyl-L-valyl-L-cysteinyl-3-(naphthalenyl)- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE

MF C63 H81 N11 O9 S2

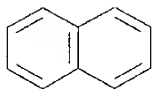
CI IDS

SR CA

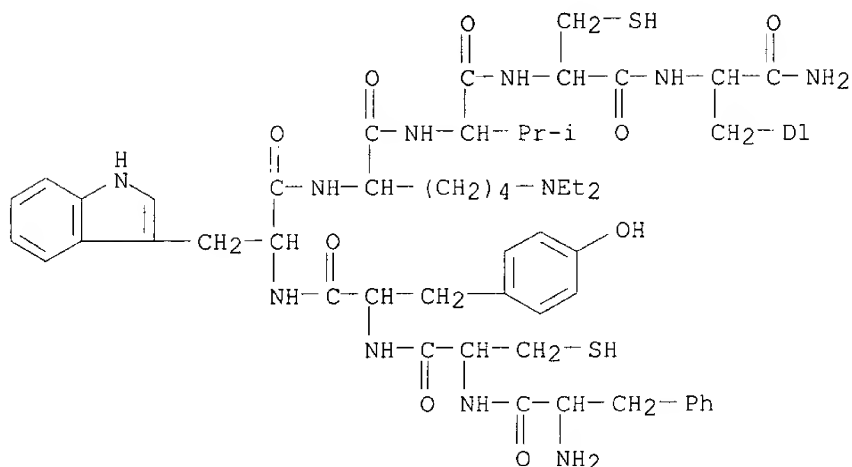
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

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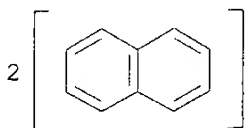
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REFERENCE 1: 120:290830

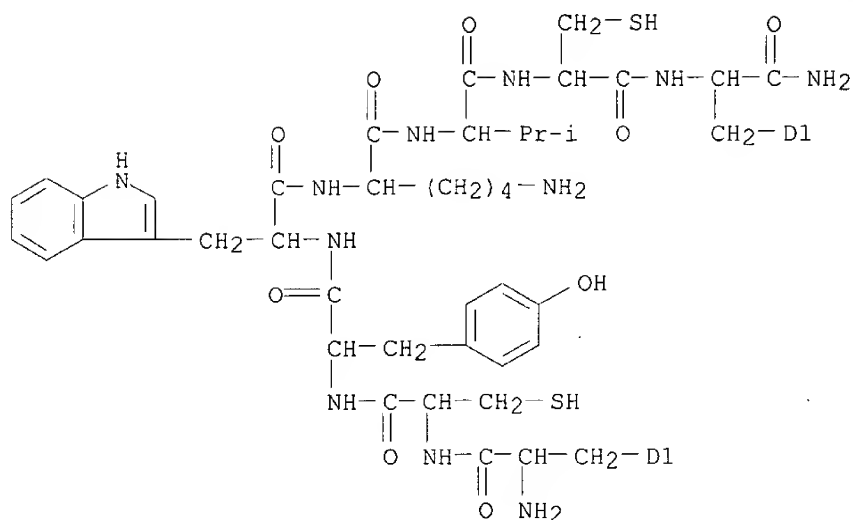
L10 ANSWER 145 OF 191 REGISTRY COPYRIGHT 2003 ACS
RN 154897-04-8 REGISTRY
CN L-Alaninamide, 3-(naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-D-cysteinyl-3-(naphthalenyl)- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF C63 H75 N11 O9 S2
CI IDS
SR CA
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

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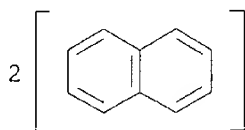
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1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

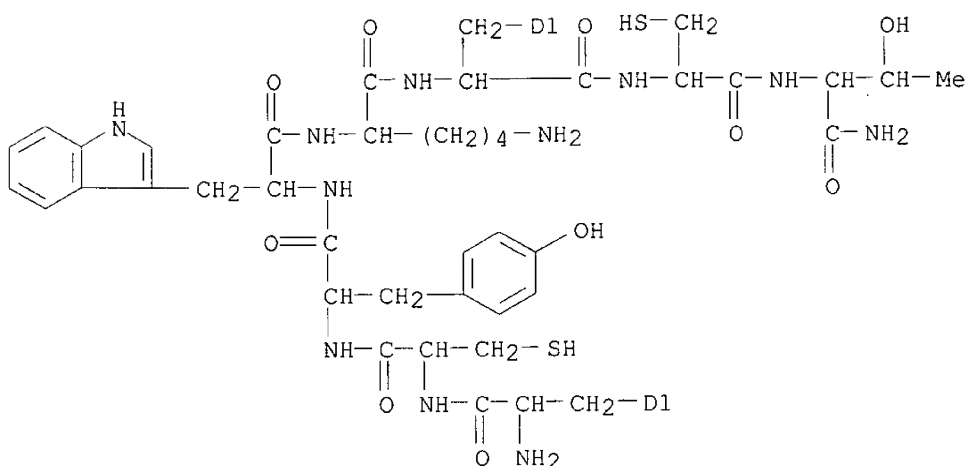
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L10 ANSWER 150 OF 191 REGISTRY COPYRIGHT 2003 ACS
RN **154896-99-8** REGISTRY
CN L-Threoninamide, 3-(naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-3-(naphthalenyl)-L-alanyl-L-cysteinyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF C62 H73 N11 O10 S2
CI IDS
SR CA
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

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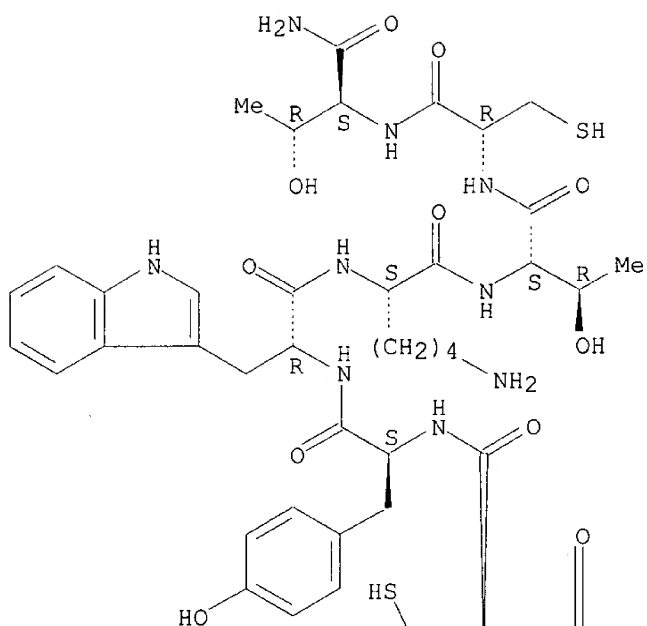
REFERENCE 1: 120:290830

L10 ANSWER 155 OF 191 REGISTRY COPYRIGHT 2003 ACS
RN **150996-95-5** REGISTRY
CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C53 H69 N11 O11 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

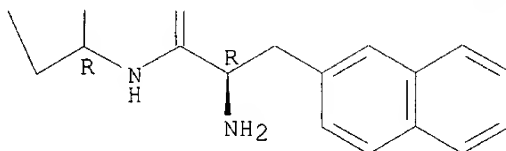
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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3 REFERENCES IN FILE CA (1957 TO DATE)
3 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 132:141955

REFERENCE 2: 128:226683

REFERENCE 3: 119:217391

L10 ANSWER 160 OF 191 REGISTRY COPYRIGHT 2003 ACS

RN 139668-84-1 REGISTRY

CN L-Threoninamide, D-phenylalanyl-S-[(4-methylphenyl)methyl]-L-cysteinyl-O-
[[(2-bromophenyl)methoxy]carbonyl]-L-tyrosyl-D-tryptophyl-N6-[[(2-
chlorophenyl)methoxy]carbonyl]-L-lysyl-L-valyl-S-[(4-methylphenyl)methyl]-
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MF C89 H101 Br Cl N11 O14 S2

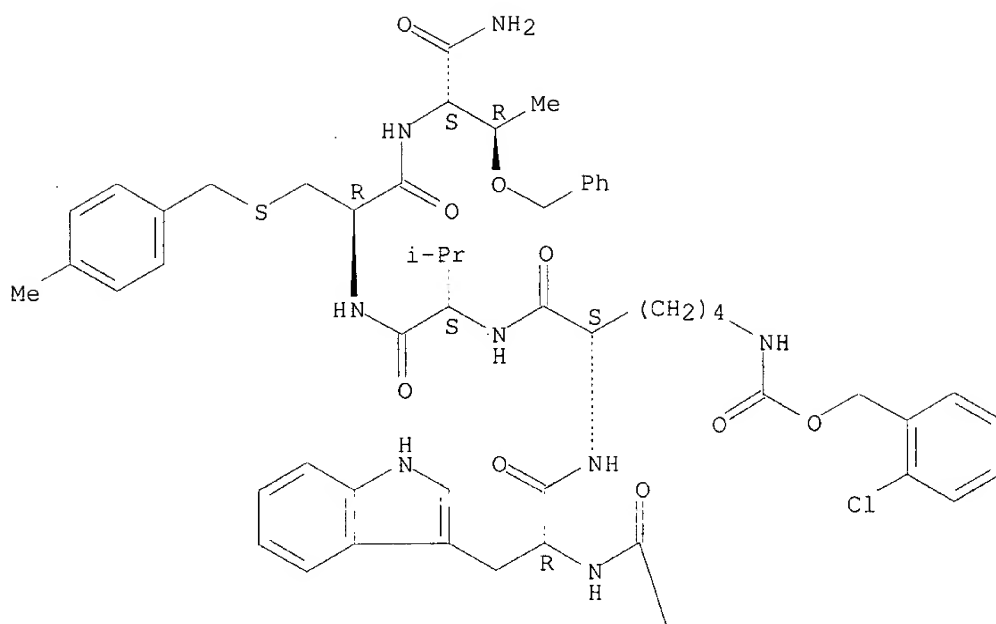
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

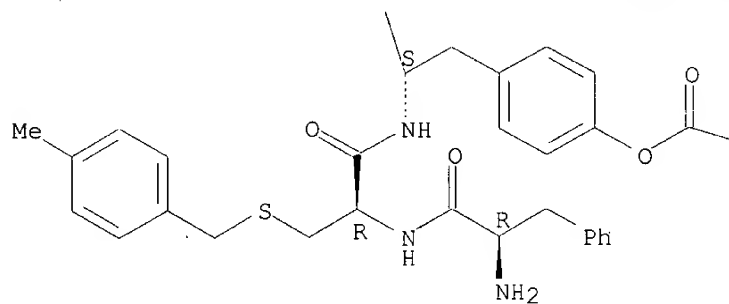
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

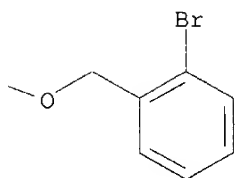
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 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 116:152405

L10 ANSWER 165 OF 191 REGISTRY COPYRIGHT 2003 ACS
 RN 132609-33-7 REGISTRY
 CN L-Threoninamide, 3-(1-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl- (9CI) (CA INDEX NAME)

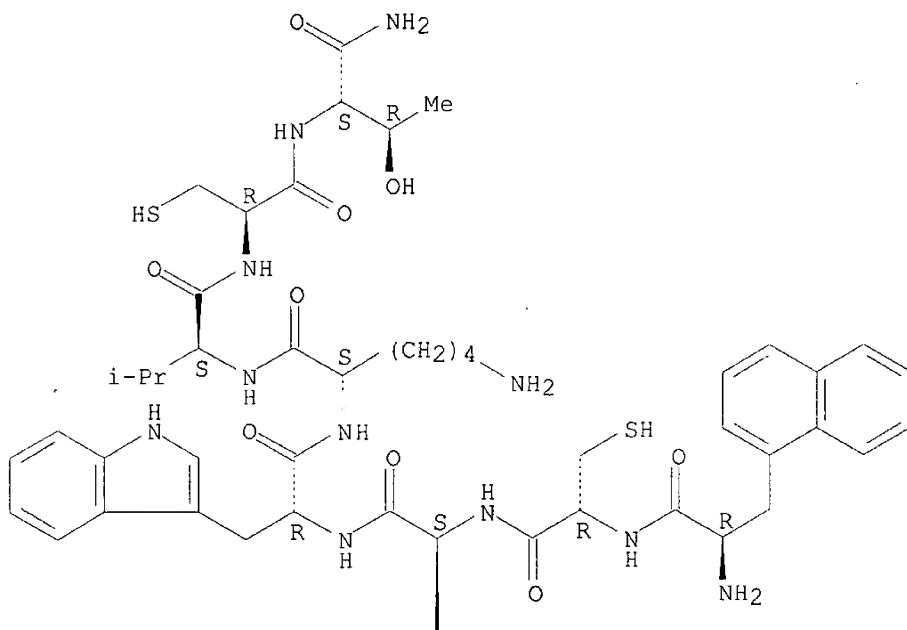
OTHER NAMES:

CN Lantreotide
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C54 H71 N11 O10 S2
 SR CA
 LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

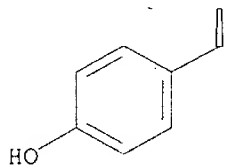
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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 5 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:180916

REFERENCE 2: 137:114538

REFERENCE 3: 135:348868

REFERENCE 4: 121:4151

REFERENCE 5: 114:143995

L10 ANSWER 170 OF 191 REGISTRY COPYRIGHT 2003 ACS

RN **117382-75-9** REGISTRY

CN L-Threoninamide, N-acetyl-4-chloro-D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-2-aminobutanoyl-L-cysteinyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

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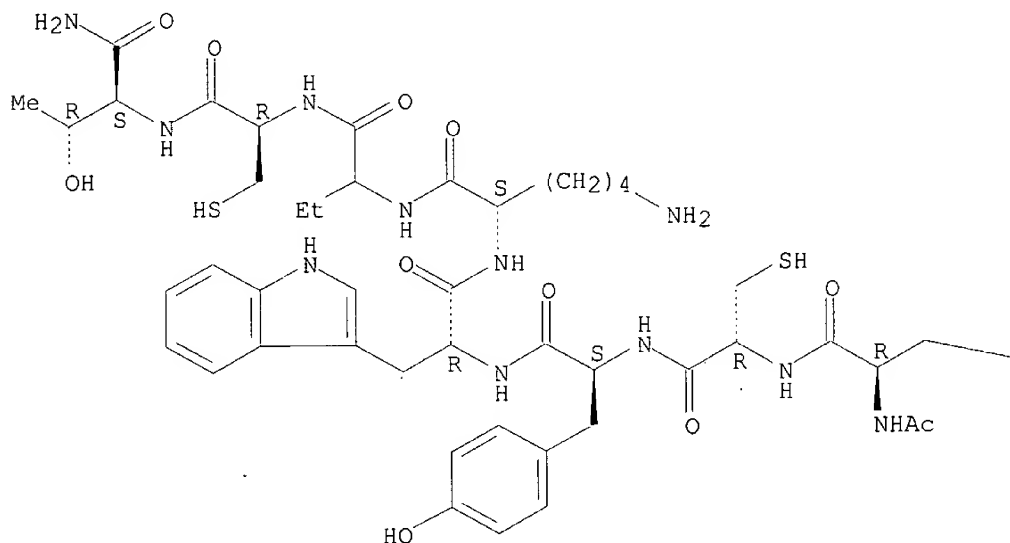
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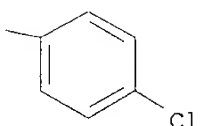
LC STN Files: CA, CAPLUS

****RELATED SEQUENCES AVAILABLE WITH SEQLINK****

Absolute stereochemistry.

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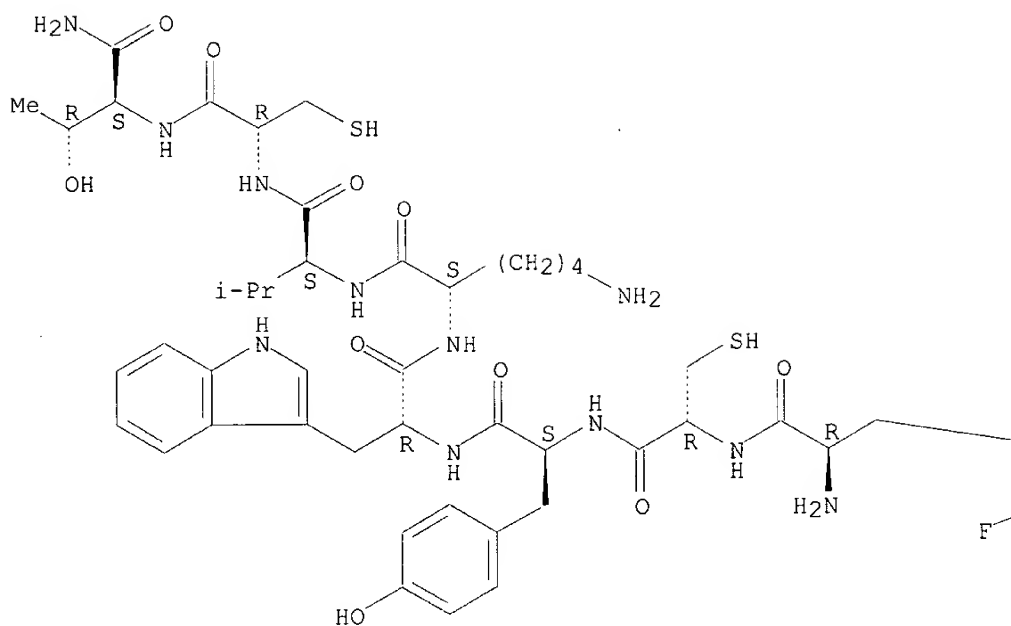
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REFERENCE 1: 109:211493

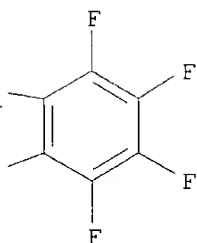
L10 ANSWER 175 OF 191 REGISTRY COPYRIGHT 2003 ACS
RN **113294-83-0** REGISTRY
CN L-Threoninamide, 2,3,4,5,6-pentafluoro-D-phenylalanyl-L-cysteiny-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteiny-L- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C50 H64 F5 N11 O10 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

****RELATED SEQUENCES AVAILABLE WITH SEQLINK****

Absolute stereochemistry.



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3 REFERENCES IN FILE CAPLUS (1957 TO DATE)

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REFERENCE 2: 128:226683

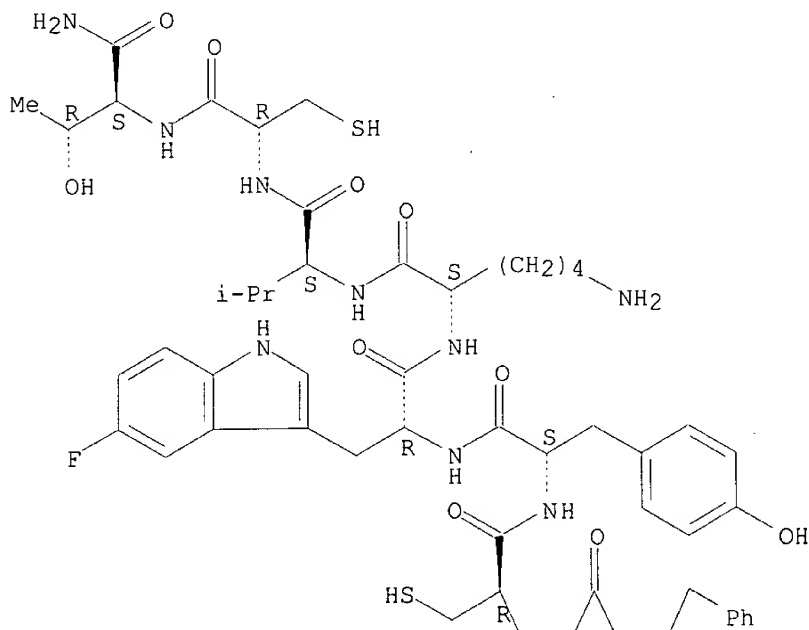
REFERENCE 3: 108:132324

L10 ANSWER 180 OF 191 REGISTRY COPYRIGHT 2003 ACS
 RN 109985-54-8 REGISTRY
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 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C50 H68 F N11 O10 S2
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

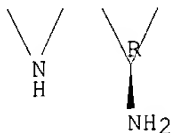
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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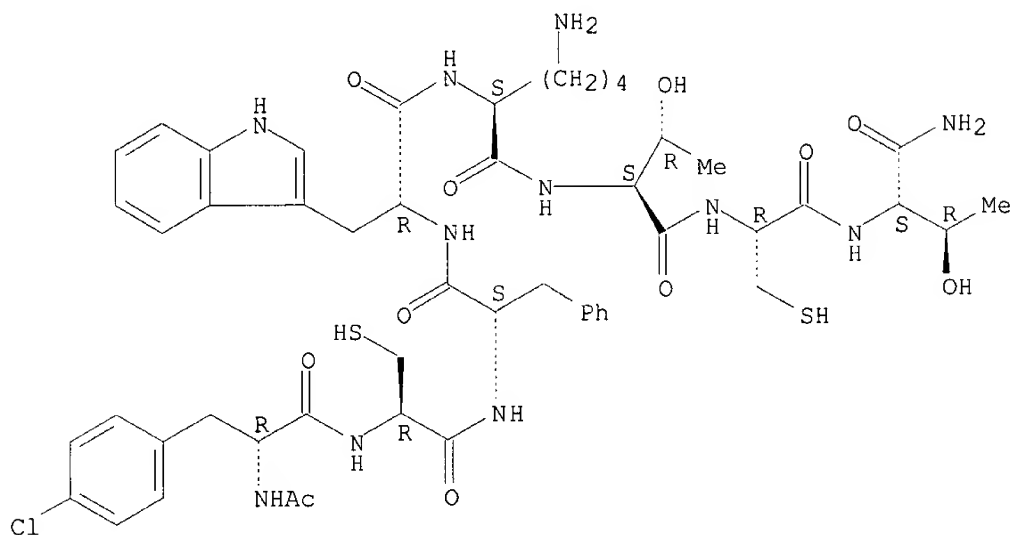
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L10 ANSWER 185 OF 191 REGISTRY COPYRIGHT 2003 ACS
 RN 109985-47-9 REGISTRY
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 FS PROTEIN SEQUENCE; STEREOSEARCH

MF C51 H68 Cl N11 O11 S2
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



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 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

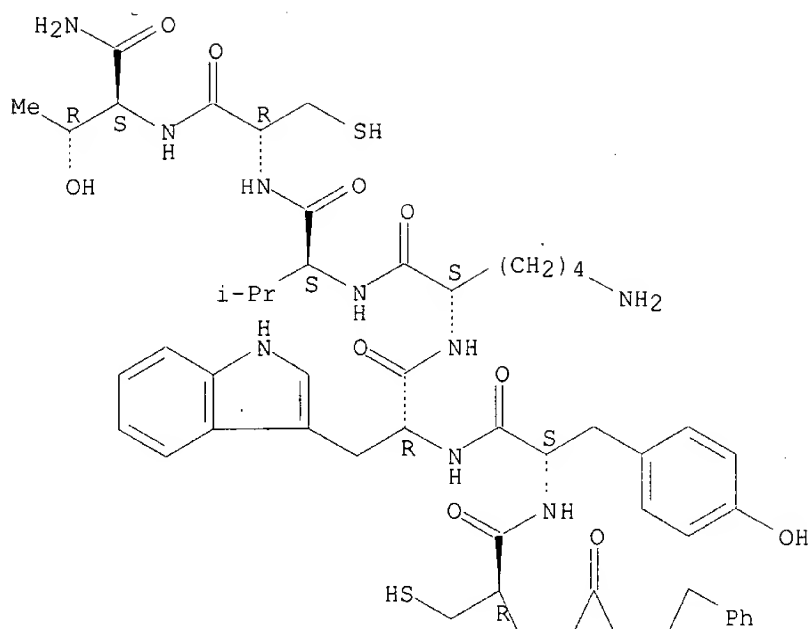
REFERENCE 1: 107:115974

L10 ANSWER 190 OF 191 REGISTRY COPYRIGHT 2003 ACS
 RN 103222-03-3 REGISTRY
 CN L-Threoninamide, D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl- (9Cl) (CA INDEX NAME)
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C50 H69 N11 O10 S2
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

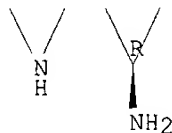
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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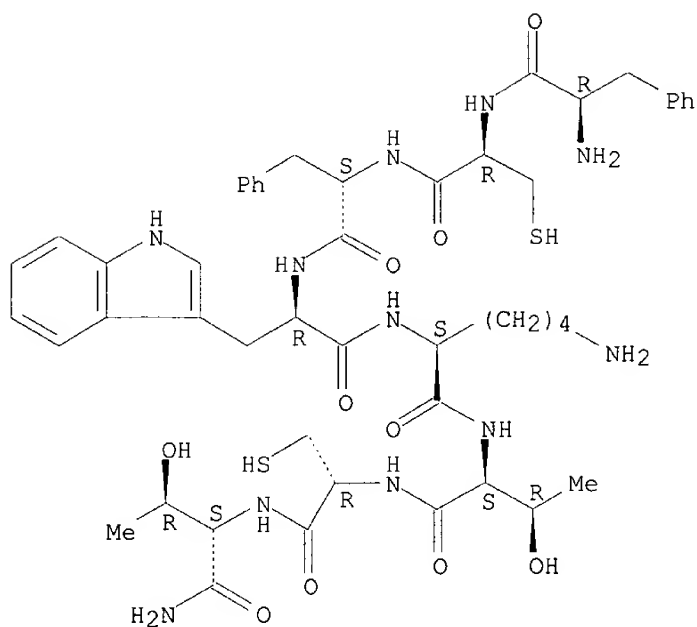
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5 REFERENCES IN FILE CAPLUS (1957 TO DATE)

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REFERENCE 3: 111:50777
REFERENCE 4: 107:115974
REFERENCE 5: 105:72825

L10 ANSWER 191 OF 191 REGISTRY COPYRIGHT 2003 ACS
RN 95833-38-8 REGISTRY
CN L-Threoninamide, D-phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C49 H67 N11 O10 S2
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



4 REFERENCES IN FILE CA (1957 TO DATE)
4 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 131:295567
REFERENCE 2: 128:280377
REFERENCE 3: 128:226683
REFERENCE 4: 102:160733